Journal of the American College of Cardiology
© 2005 by the American College of Cardiology Foundation
Published by Elsevier Inc.

Vol. 45, No. 2, 2005
ISSN 0735-1097/05/$30.00
doi:10.1016/j.jacc.2004.10.034

Health-Related Quality of Life After Interventional or Conservative Strategy in Patients With Unstable Angina or Non–ST-Segment Elevation Myocardial Infarction

One-Year Results of the Third Randomized Intervention Trial of Unstable Angina (RITA-3)

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OBJECTIVES We sought to compare the effects of an early interventional strategy (IS) versus a conservative strategy (CS) on health-related quality of life (HRQOL) in patients with non–ST-segment elevation acute coronary syndromes (ACS).

BACKGROUND The third Randomized Intervention Trial of unstable Angina (RITA-3) evaluated early IS (n = 895) versus CS (n = 915). We report one-year results of the RITA-3 trial concerning HRQOL.

METHODS The patients' HRQOL was assessed with the Short Form-36 (SF-36) and Seattle Angina Questionnaire (SAQ) at four-month and one-year follow-up, and the EuroQOL Visual Analogue Scale (EQ-VAS) and EuroQOL 5-Dimensional Classification (EQ-5D) also measured at baseline. Analysis was performed using the two-sample *t* test and analysis of co-variance.

RESULTS Mean changes from baseline EQ-VAS scores were better for IS than for CS at four months (treatment difference of 3.0, $p < 0.001$) and one year (2.3, $p < 0.01$). The EQ-5D utility scores were also higher for IS at four months (treatment difference: 0.036, $p < 0.01$) and at one year (0.016, $p = 0.20$). For SF-36, IS scored significantly better at four months for physical function, physical role function, emotional role function, social function, vitality, and general health. The SAQ scores for exertional capacity, anginal stability and frequency, treatment satisfaction, and disease perception were better for IS at four months. These treatment differences were present but attenuated by one-year follow-up. Improvements in HRQOL for IS could be attributed to improvements in anginal symptoms.

CONCLUSIONS In patients with non–ST-segment elevation ACS, an early IS provides greater gains in HRQOL, as compared with CS, mainly due to improvements in angina grade. (J Am Coll Cardiol 2005;45:221–8) © 2005 by the American College of Cardiology Foundation

The use of an early interventional strategy in the management of patients with unstable coronary artery disease has been controversial (1,2). The third Randomized Intervention Trial of unstable Angina (RITA-3) was performed to compare an early interventional strategy (IS) with a conservative strategy (CS) in the treatment of patients with unstable angina or non–ST-segment elevation myocardial infarction (MI) (3). At four-month follow-up, patients randomized to an early IS had a lower risk of developing the combined end point of refractory angina, nonfatal MI, or death. At one year, the treatment groups were comparable with respect to the combined end point of death or nonfatal MI.

Although the clinical benefits of an early IS appear to be clear, its effects on health-related quality of life (HRQOL) remain uncertain. The HRQOL is of particular concern in studies, such as the RITA-3 trial, for which there is a marked difference in the invasiveness of the therapeutic options being considered. In this report, we present our findings from the RITA-3 trial with regard to the effects of an early IS on HRQOL.

METHODS

The RITA-3 trial. Details of the design and protocol of the RITA-3 trial are described elsewhere (3). Briefly, patients were recruited from 45 centers across England and

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Manuscript received June 7, 2004; revised manuscript received September 16, 2004, accepted October 4, 2004.

JACC Vol. 45, No. 2, 2005
January 18, 2005:221–8

Abbreviations and Acronyms

ACS = acute coronary syndrome
CS = conservative strategy
CCS = Canadian Cardiovascular Society
HRQOL = health-related quality of life
IS = interventional strategy
EQ-5D = EuroQOL 5-Dimensional Classification
EQ-VAS = EuroQOL Visual Analogue Scale
MI = myocardial infarction
RITA-3 = third Randomized Intervention Trial of unstable Angina
SAQ = Seattle Angina Questionnaire
SF-36 = Short Form-36

Scotland from November 12, 1997 to October 2, 2001. Patients were eligible for the study if they experienced chest pain at rest and had documented electrocardiographic or previous arteriographic evidence of coronary artery disease. Patients were randomized either to an early IS (i.e., maximal medical therapy plus early coronary arteriography with possible myocardial revascularization) or to a more CS (i.e., maximal medical therapy plus ischemia- or symptom-provoked angiography and revascularization). Among patients randomized to CS, 94 (10%) of 915 patients had a revascularization procedure during the index admission, compared with 397 (44%) of 895 patients in the IS group (3). Within one year, 28% and 57% of patients in the CS and IS groups were revascularized, respectively.

In all eligible patients, the optimal treatment strategy was uncertain. The co-primary end points of the study were a composite of death, nonfatal MI, or refractory angina at four-month follow-up and a composite of death or nonfatal MI at one-year follow-up.

Health-related quality-of-life instruments. The HRQOL was assessed using both generic and disease-specific self-administered questionnaires: the EuroQOL Visual Analogue Scale (EQ-VAS), EuroQOL 5-Dimensional Classification (EQ-5D), Short Form-36 (SF-36), and Seattle Angina Questionnaire (SAQ) (4–6). Four-month and one-year assessments were performed on all HRQOL instruments, and the two components of the EuroQOL questionnaire were also completed at baseline. The results of HRQOL are confined to those patients who survived to the end of the study period.

The EuroQOL is a two-part, preference-based, generic, self-reported questionnaire composed of the EQ-5D health classification and the EQ-VAS (7). The EQ-VAS is a 20-cm visual analogue scale ranging from 0 (worst imaginable health state) to 100 (best imaginable health state) on which patients are asked to grade their current state of health. An advantage of the EQ-VAS is its relative ease of use and interpretation, although this advantage is offset by the lack of specificity concerning the particular aspect of HRQOL being measured.

The EQ-5D assesses five dimensions of HRQOL: mobility, self-care, usual activities, pain or discomfort, and anxiety or depression. Each dimension is measured on a 3-point ordinal scale where a higher score corresponds to a worse health state (no limitation, some limitation, and greatest limitation in HRQOL). A strength of the EQ-5D is that through their response, patients can effectively locate themselves into one of 245 possible health states for which a global value (i.e., a "utility score") is assigned. The utility score has been previously determined based on the preferences of a sample of 3,395 members of the United Kingdom general population (8). A utility score of 1 corresponds to the highest degree of HRQOL, and score of 0 is compatible with a level of HRQOL equivalent to death. A negative score indicates a state of HRQOL that is worse than death. The EuroQOL questionnaire has been previously validated in various settings (9–12).

The SF-36 is a generic HRQOL instrument consisting of 36 items grouped into eight dimensions: physical functioning (10 items), physical role functioning (4 items), emotional role functioning (3 items), social functioning (2 items), bodily pain (2 items), mental health (5 items), vitality (4 items), general health perceptions (5 items), and the patient's change in health as compared with one year ago (not considered for this study) (6). Each dimension is scaled on a continuum and ranges from 0 (worst imaginable health state) to 100 (best imaginable health state). The SF-36 has been previously validated in patients with ischemic disease and in the British general population (13–16).

The SAQ is a 19-item, disease-specific questionnaire designed to assess five dimensions of HRQOL related to angina: exertional capacity, angina stability, angina frequency, treatment satisfaction, and disease perception (5). Each component is scaled on a continuum from 0 (worst possible health state) to 100 (best possible health state). An advantage of the SAQ is the high degree of specificity for which it captures HRQOL related to angina (5). The SAQ has been previously validated and applied in patients with ACS (5,17–21).

Although individuals with nonresponses to entire questionnaires were excluded from the analysis, we included those with partial responses where possible. A nonresponse to a particular question did not contribute to the calculation of the component scores.

Other measurements. Angina grade was assessed according to the Canadian Cardiovascular Society (CCS) classification at baseline and all subsequent follow-up visits (22). We modified the CCS scheme for this study to include 0 to indicate the absence of angina. Breathlessness was evaluated on a 6-point ordinal scale: not breathless, breathless while climbing hills, breathless while hurrying on the level, breathless while walking at own pace, breathless while dressing or washing, and breathless at rest (3). Physical activity level was measured on a five-point scale: inactive, sedentary, mild activity level, moderate activity level, and vigorous activity level.

Statistical analysis. Analysis of covariance was used to assess possible treatment differences in change from baseline scores for the EQ-VAS score and EQ-5D global utility

Table 1. Response Rates by Health-Related Quality-of-Life Questionnaire

	Baseline		4 Months		1 Year	
Questionnaire	**IS**	**CS**	**IS**	**CS**	**IS**	**CS**
Total alive	895	915	869	892	854	879
Died	—	—	26	23	41	36
EQ-VAS	887 (99%)	912 (99%)	839 (97%)	852 (96%)	805 (94%)	817 (93%)
EQ-5D	886 (99%)	912 (99%)	839 (97%)	853 (96%)	806 (94%)	820 (93%)
SF-36	—	—	841 (97%)	854 (96%)	805 (94%)	822 (94%)
SAQ	—	—	839 (97%)	855 (96%)	804 (94%)	817 (93%)

All percentages were calculated as a proportion of total patients alive. The Short Form-36 (SF-36) and Seattle Angina Questionnaire (SAQ) were not administered at baseline.

CS = conservative strategy (n = 915); EQ-5D = EuroQOL 5-Dimensional Classification; EQ-VAS = EuroQOL Visual Analogue Scale; IS = interventional strategy (n = 895).

score. The two-sample *t* test was used to assess treatment differences for the SF-36 and SAQ. For the EQ-5D, a test of linear trend was performed to evaluate a change from baseline scores between the treatment groups. A p value of <0.05 was considered to be statistically significant. Unless stated otherwise, Bonferroni adjustment was applied in the calculation of treatment differences for each component score in order to correct for having two repeated measures performed at four-month and one-year follow-up. Data are presented as the mean value ± SE, unless otherwise stated. All statistical analyses were performed using STATA (Version 8.2, College Station, Texas).

RESULTS

A total of 1,810 patients were randomized to early IS (n = 895) or CS (n = 915). Response rates for all HRQOL questionnaires were high, as well as being comparable between treatment groups (Table 1). Responses to individual HRQOL questions ranged from 95% to 99% complete.

EuroQOL. Baseline EQ-VAS scores were comparable between IS and CS patients (Fig. 1). At four months, patients in both the IS group and CS groups experienced a significant increase in mean VAS scores from baseline

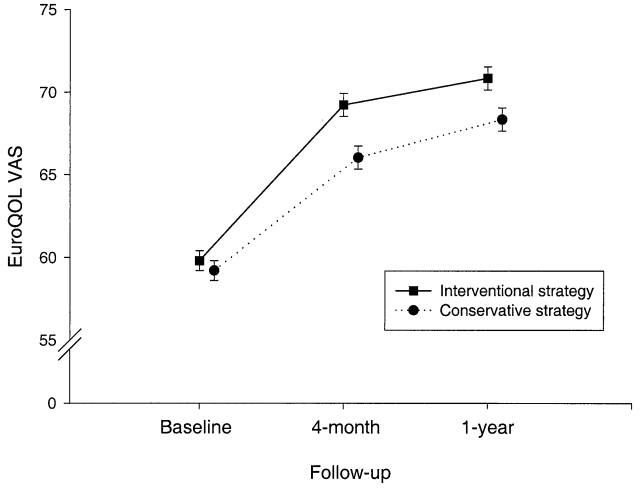

Figure 1. Mean ± SEM values of EuroQOL-Visual Analogue Scale (VAS) at baseline and four-month and one-year follow-up by treatment group. Results for the conservative strategy group are offset for clarity.

(mean differences of 9.2 from baseline, 95% confidence interval [CI] 8.0 to 10.4; and 6.2, 95% CI 5.0 to 7.4, respectively). The improvement at four months was significantly greater in the IS group compared with the CS group (mean difference of 3.0, 95% CI 1.3 to 4.7; $p < 0.001$). Results for one-year follow-up showed a further increase in mean VAS scores in both treatment groups, but the treatment difference was slightly less (mean difference of 2.3, 95% CI 0.6 to 4.1; $p < 0.01$).

Table 2 shows the frequency of individuals who had a change in EQ-5D score from baseline at four months and at one year (reported p values for trend were not corrected for multiple comparisons). For the most part, there was no difference in change from baseline scores between the treatment groups. However, at both follow-up times, a larger percentage of patients in the CS group had a worsening of HRQOL related to performing usual daily activities. More patients in the CS group also had poorer HRQOL due to anxiety at four months.

With regard to the EQ-5D global utility score (Table 3), patients in both treatment groups experienced a highly significant increase in HRQOL from baseline to four months, as well as from baseline to one year. Although the change in the global utility score was significantly better among patients in the IS group at four months (treatment mean difference of 0.036, $p = 0.005$), this difference was reduced by one year (treatment mean difference of 0.016, $p = 0.20$).

SF-36. All of the mean SF-36 component scores were better for patients in the IS group than in the CS group (Table 4). At four months, all of the treatment differences were statistically significant, with the exception of bodily pain and mental health. At one year, these differences were attenuated but remained statistically significant for physical role function, social function, vitality, and general health. At both follow-up times, the largest gains in HRQOL were made with regard to physical role function and general health.

SAQ. The mean SAQ component scores were significantly better in the IS group than in the CS group (Table 5). The treatment differences for one-year follow-up were attenuated, as compared with the four-month results, but re-

Table 2. EuroQOL 5-Dimensional Classification Component Scores and Global Utility Score

EQ-5D Component Change From Baseline	4 Months			1 Year		
	IS	CS	p Value for Trend	IS	CS	p Value for Trend
Mobility						
Improved	193 (23%)	196 (23%)	0.78	182 (23%)	201 (24%)	0.41
No change	545 (65%)	550 (64%)		507 (63%)	511 (62%)	
Worsened	101 (12%)	109 (13%)		115 (14%)	112 (14%)	
Self-care						
Improved	74 (9%)	75 (8%)	0.37	75 (9%)	73 (9%)	0.39
No change	707 (84%)	705 (83%)		673 (84%)	683 (83%)	
Worsened	58 (7%)	74 (9%)		56 (7%)	68 (8%)	
Usual activities						
Improved	227 (27%)	195 (23%)	0.01	233 (29%)	212 (26%)	0.04
No change	491 (59%)	504 (59%)		451 (56%)	459 (56%)	
Worsened	119 (14%)	153 (18%)		120 (15%)	151 (18%)	
Pain or discomfort						
Improved	140 (17%)	142 (17%)	0.07	130 (16%)	150 (18%)	0.87
No change	506 (60%)	470 (55%)		479 (60%)	453 (55%)	
Worsened	190 (23%)	241 (28%)		192 (24%)	218 (27%)	
Anxiety						
Improved	190 (22%)	179 (21%)	0.03	202 (25%)	195 (24%)	0.36
No change	523 (63%)	507 (59%)		482 (60%)	496 (60%)	
Worsened	123 (15%)	167 (20%)		118 (15%)	132 (16%)	

Scores are relative to baseline scores. The reported p values for trend were not corrected for multiple comparisons.
Abbreviations as in Table 1.

mained highly significant. The largest gains in HRQOL were related to anginal stability, anginal frequency, and disease perception.

Relation of angina grade to HRQOL. As previously reported (3), there were substantial treatment differences in angina grade. At four months, the prevalences of grade 2 or higher were 26.3% and 36.3% in the IS and CS groups, respectively (difference of 10%, $p < 0.0001$); at one year, this difference was 7.6% ($p = 0.0006$). The frequency of angina grade among those who completed the EQ-VAS questionnaire is shown in Table 6.

To evaluate whether the effect of treatment on HRQOL was explained by treatment differences in angina grade, we compared the mean EQ-VAS scores between treatment groups after classifying patients according to current angina grade (Fig. 2). The figure shows a marked decline in HRQOL with increasing severity of angina in both treatment groups. However, at four months and one year, patients with the same angina grade in their respective treatment groups had similar HRQOL. Thus, the gain in HRQOL achieved with an early IS appears to be largely explained by the improvement of angina grade.

Similar results were obtained with the SF-36 (results not shown), where all of the treatment differences became comparable after stratification by angina grade. The only exceptions were observed at four months among those with CCS angina grade 0, who had significant treatment differences for vitality (mean treatment difference of 4.0, $p = 0.006$) and general health (mean treatment difference of 4.5, $p = 0.002$).

DISCUSSION

Our findings suggest that in patients with unstable angina or non–ST-segment elevation MI, an early IS provides greater improvements in HRQOL than does a more CS. The gains achieved with early IS appear to be explained at least in part by improvements in angina grade. We found that treatment differences diminished over time; however, this apparent attenuation may be explained by the use of nonrandomized intervention in some patients assigned to

Table 3. EuroQOL 5-Dimensional Classification Global Utility Score

	4 Months		1 Year	
	IS	CS	IS	CS
Mean ± SE	0.748 ± 0.009	0.714 ± 0.010	0.752 ± 0.009	0.736 ± 0.010
Difference from baseline*	0.077 ± 0.009	0.041 ± 0.009	0.079 ± 0.009	0.063 ± 0.009
Treatment difference (95% CI)	0.036 (0.011–0.061)		0.016 (−0.009–0.042)	

*In responding to the EQ-5D, patients effectively locate themselves into one of 245 possible health states for which a global value or "utility" has been previously estimated based on a standard population. A utility score of 1 corresponds to the highest degree of HRQOL, and score of 0 is compatible with a level of HRQOL considered equivalent to death. A negative score suggests a state of HRQOL that is worse than death. Bonferroni adjustment was applied for each component score to correct for repeated measures at 4-month and 1-year follow-up.
CI = confidence interval; other abbreviations as in Table 1.

Table 4. Short Form-36 Component Scores at Four-Month and One-Year Follow-Up

	IS (Mean ± SE)	CS (Mean ± SE)	Difference (IS–CS)		
			Mean Value	*t*	p Value
4 Months					
Physical function	63.0 ± 1.0	59.3 ± 1.0	3.7	2.7	<0.01
Physical role function	51.7 ± 1.5	44.9 ± 1.5	6.8	3.3	<0.01
Emotional role function	72.0 ± 1.4	67.1 ± 1.4	4.9	2.5	0.01
Social function	73.4 ± 1.0	69.7 ± 1.0	3.7	2.6	0.01
Bodily pain	63.4 ± 1.0	61.7 ± 1.0	1.7	1.2	0.22
Mental health	72.4 ± 0.7	70.6 ± 0.7	1.8	1.8	0.07
Vitality	52.3 ± 0.8	47.7 ± 0.8	4.6	4.0	<0.0001
General health	59.5 ± 0.8	54.4 ± 0.8	5.1	4.6	<0.0001
1 Year					
Physical function	62.5 ± 1.0	61.0 ± 1.0	1.5	1.0	0.31
Physical role function	57.0 ± 1.5	52.4 ± 1.5	4.6	2.1	0.03
Emotional role function	74.9 ± 1.4	72.4 ± 1.4	2.5	1.3	0.20
Social function	76.9 ± 1.0	72.9 ± 1.0	4.0	2.8	0.01
Bodily pain	65.2 ± 1.0	64.1 ± 1.0	1.1	0.8	0.44
Mental health	74.3 ± 0.7	72.5 ± 0.7	1.8	1.8	0.07
Vitality	52.9 ± 0.9	50.3 ± 0.9	2.6	2.1	0.03
General health	59.4 ± 0.8	55.4 ± 0.8	4.0	3.3	<0.001

Each SF-36 component score is continuous and ranges from 0 to 100 (a higher score is consistent with better HRQOL). A score of 0 suggests the lowest possible HRQOL; a score of 100 suggests the greatest possible HRQOL. "Physical function" is defined as the extent to which health limits physical activities, such as self-case, walking climbing stairs, etc. "Physical role functioning" is defined as the extent to which physical health interferes with work or other daily activities such as accomplished less than wanted, limitations in the kind of activities, etc. Bonferront adjustment was applied for each component score to correct for repeated measures at 4-month and 1-year follow-up.

Abbreviations as in Table 1.

the CS group. It is likely that the observed attenuation in HRQOL scores at one year reflects those severely symptomatic patients in the conservative arm who crossed over and underwent revascularization and hence, were likely to have benefits in HRQOL.

Response rates for all HRQOL instruments used in this study were high (at least 93%) and comparable across treatment groups. Only one patient was lost during the entire course of follow-up. Thus, it is unlikely that our findings were due to bias resulting from differential response rates or losses to follow-up. Overall, baseline clinical characteristics were comparable between patients with and without follow-up of HRQOL scores (results not shown).

An advantage of using a generic HRQOL instrument, such as the EQ-VAS, is ease of use (23). It also provides information on a patient's global state of well-being and allows comparability of relative health states across different diseases (6). However, disease-specific instruments provide greater sensitivity for detecting small changes in HRQOL and give further details on the influence of various components of a particular disease on HRQOL (24). The results of our study were in line with these expectations, where the largest treatment differences in HRQOL were found with the SAQ.

Comparison of results against previous studies. Overall, our findings are consistent with those of previous studies

Table 5. Seattle Angina Questionnaire Components at Four-Month and One-Year Follow-Up

	IS (Mean ± SE)	CS (Mean ± SE)	Difference (IS–CS)		
			Mean Value	*t*	p Value
4 Months					
Exertional capacity	75.4 ± 0.9	69.8 ± 0.9	5.6	4.2	<0.0001
Anginal stability	70.3 ± 1.0	63.9 ± 1.0	6.4	4.5	<0.0001
Anginal frequency	80.2 ± 0.9	72.6 ± 0.9	7.6	5.7	<0.0001
Treatment satisfaction	90.1 ± 0.5	86.3 ± 0.5	3.8	4.9	<0.0001
Disease perception	72.1 ± 0.9	64.4 ± 0.8	7.7	6.2	<0.0001
1 Year					
Exertional capacity	76.9 ± 1.0	73.3 ± 1.0	3.6	2.7	<0.01
Anginal stability	67.7 ± 1.0	63.7 ± 1.0	4.0	3.0	<0.01
Anginal frequency	82.4 ± 0.9	78.0 ± 0.9	4.4	3.4	<0.001
Treatment satisfaction	91.2 ± 0.5	88.6 ± 0.5	2.6	3.6	<0.001
Disease perception	75.9 ± 0.9	71.2 ± 0.9	4.7	4.1	<0.0001

Each SAQ component score is continuous and ranges from 0 to 100 (a higher score is consistent with better HRQOL). A score of 0 suggests the lowest possible HRQOL; a score of 100 suggests the greatest possible HRQOL. Bonferroni adjustment was applied for each component score to correct for repeated measures at 4-month and 1-year follow-up.

Abbreviations as in Table 1.

Table 6. Distribution of Angina Grade by Treatment Group and Follow-Up Among Patients Who Completed a EuroQOL Questionnaire

Follow-Up Treatment	CCS Angina Grade at Baseline				
	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4
4 Months					
IS	556 (66%)	64 (8%)	107 (13%)	52 (6%)	60 (7%)
CS	462 (54%)	75 (9%)	152 (18%)	56 (6%)	107 (13%)
1 Year					
IS	542 (67%)	71 (9%)	89 (11%)	41 (5%)	61 (8%)
CS	487 (60%)	80 (10%)	111 (13%)	50 (6%)	89 (11%)

CCS = Canadian Cardiovascular Society; other abbreviations as in Table 1.

that compared an interventional therapy (i.e., percutaneous transluminal coronary angiography [PTCA], stenting, or coronary artery bypass graft surgery [CABG]) against a more conservative therapy (i.e., medical therapy or symptom-provoked revascularization). Among studies that used the SF-36, it was reported that patients who received an interventional therapy had a significantly better HRQOL related to physical functioning (25–27), physical role functioning (27), general health (25,28), and vitality (25,28). Some studies also found that an interventional therapy provided greater improvements in HRQOL related to bodily pain (28) and mental health (26). In studies where baseline scores were measured, the authors reported significant improvements in at least one of the SF-36 components over time (25,26,28).

With respect to the SAQ, Rinfret et al. (29) reported better HRQOL in patients who underwent stenting compared with those who underwent PTCA with regard to anginal frequency, bodily pain, and disease perception. However, Weaver et al. (30) found no treatment difference in HRQOL between patients who underwent stenting versus balloon angioplasty. The Stent or Surgery Trial (31) compared HRQOL in patients randomized to CABG or PTCA and found that patients in the CABG group had greater improvements in exercise capacity, angina frequency, and disease perception.

In a retrospective cohort study, Sollano et al. (32) compared HRQOL using the EuroQOL in patients who underwent CABG with those who received standard medical therapy. It was reported that the CABG group had better EQ-5D global utility scores than did the medical therapy group. However, in a randomized study that compared stenting to CABG, Serruys et al. (33) found no treatment difference in EQ-VAS or in the EQ-5D global utility index at six-month and one-year follow-up. At one-year follow-up, however, the CABG group had better EQ-5D scores related to usual activities and anxiety.

The results of our study were also consistent with those of a validation study conducted by Dougherty et al. (24), who compared the relative merits of the SAQ (a disease-specific measure), the SF-36 (a global measure), and the Quality of Life Index-Cardiac version III (a more global measure) for capturing CCS angina grade. The authors found the same rank order of sensitivity (i.e., disease-specific, generic, and more generic) as that in our study for detecting changes in HRQOL across the three HRQOL instruments.

Clinical implications. Our findings suggest that an early IS provides small but clinically relevant improvements in HRQOL. Based on the criterion specified by Spertus et al. (34,35), which states that a clinically meaningful difference in SAQ scores ranges between 5 to 8 points, the observed four-month treatment differences for exertional capacity,

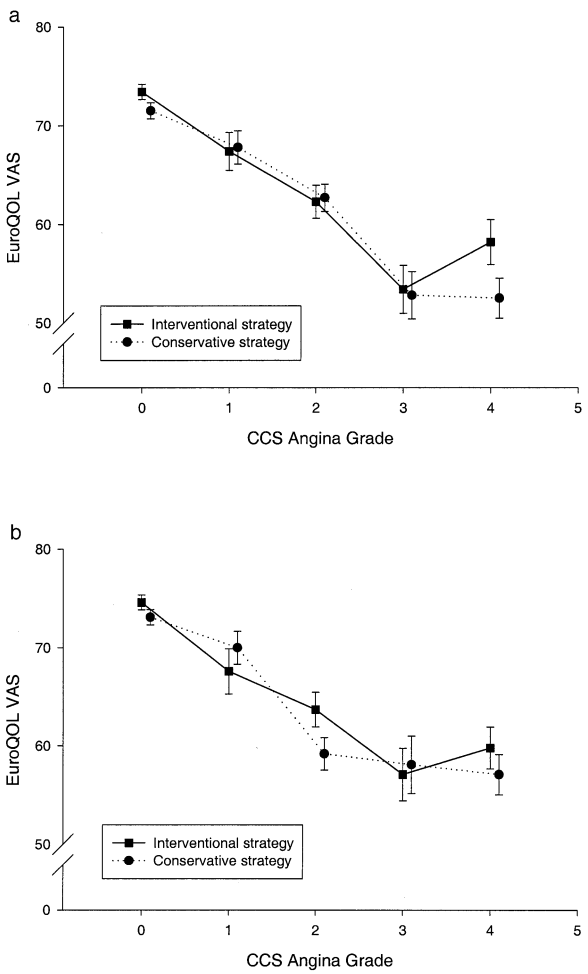

Figure 2. Mean ± SEM values of EuroQOL-Visual Analogue Scale (VAS) for patients classified by their current Canadian Cardiovascular Society (CCS) angina grade and treatment group at four months **(a)** and one-year follow-up **(b)**. Results for the conservative strategy group are offset for clarity.

anginal stability, anginal frequency, and disease perception would be considered clinically important.

In addition, we found that for each 1-unit increase in angina grade, there was about a 5-unit decline in the EQ-VAS score ($p < 0.001$). At four months, patients in the IS group had, on average, scored three points higher on EQ-VAS than those in the CS group, or about 60% of a 1-unit change in angina grade. Likewise, a 1-unit increase in angina grade corresponded to a 0.068-point decline in the EQ-5D utility score ($p < 0.001$). We found that patients in the interventional arm, on average, scored 0.036 higher on the EQ-5D utility score, or 53% of a 1-unit change in angina grade.

Clinical relevance of our HRQOL results can also be inferred from the observed difference in results between the disease-specific and generic instruments. We found that treatment differences measured using the SAQ were larger than those obtained with the EuroQOL and SF-36. For example, at four months, we found a 7.7-point difference in HRQOL related to disease perception with the SAQ, compared with a 4.6-point difference in HRQOL related to general health using the SF-36. Moreover, all of the SAQ showed highly significant differences in favor of the IS, whereas only some of the components of the generic questionnaires showed such a treatment benefit. The consistency of these findings with the reduction in the occurrence of refractory angina and CCS angina grade reported previously (3) suggests that the observed differences in HRQOL are clinically significant.

Study limitations. Patients with the severest form of angina or ischemia were excluded from this study because the inclusion criteria required continued medical therapy to be a viable treatment option. Thus, our findings may not be generalizable to those with advanced cardiac disease. In addition, baseline scores for the SF-36 and SAQ were not measured and therefore were not adjusted for in the analysis. However, baselines scores for the EuroQOL were available and found to be highly comparable, suggesting that the randomization procedure provided a balance of factors that determine HRQOL between the treatment groups.

Future directions. The main advantage of early intervention is the reduction of refractory angina at four-month and one-year follow-up (3). An early intervention conferred no advantage over a conservative strategy for death or MI. The effect of an early intervention on HRQOL was small, and the benefits related to HRQOL appeared to be attributable to improvements in angina grade. Thus, the public policy implications of this study are that an early IS should be recommended to reduce the occurrence of refractory angina and possibly to improve angina-related HRQOL in patients with non–ST-segment elevation ACS. However, this benefit must be balanced against economic cost and clinical risk of performing an early intervention on all patients.

The findings of this study, coupled with the main one-year results of the RITA-3 trial, provide evidence in favor of an early IS. However, further research is needed to evaluate the cost-effectiveness of IS compared with CS and to evaluate these results against existing studies (21,36) in order to fully assess the public health implications of these alternative treatment strategies.

Conclusions. In the management of patients with non–ST-segment ACS, an early IS provides greater improvements in HRQOL as compared with a more CS. Much of the gains in HRQOL appear to be attributable to improvements in angina grade.

Acknowledgments

We gratefully acknowledge the dedicated efforts of the investigators, the coordinators, and the volunteer patients who participated in the RITA-3 trial.

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