# Advantages of Long-Acting Antianginal Agents

*Spertus JA, Dewhurst T, Dougherty CM, Nichol P. Testing the effectiveness of converting patients to long-acting antianginal medications: The Quality of Life in Angina Research Trial (QUART). Am Heart J 2001;141:550–8.*

## Study Overview

Objective. To determine whether converting patients with stable angina to long-acting antianginal medications improves functional status, symptom control, treatment satisfaction, and quality of life when compared with usual treatment.

Design. Single-blinded (patients did not know the tested hypothesis), randomized controlled trial with a 2-week run-in period and 3 months of follow-up. Analysis was by intention to treat.

Setting and participants. The study was conducted at outpatient clinics in the Veterans Affairs Health System of Seattle, Washington. 100 patients were recruited who had documented coronary artery disease (CAD), chronic stable angina, and were taking at least 2 antianginal medications. Documented CAD was defined as prior myocardial infarction, prior coronary revascularization procedure, or a history of typical angina pectoris. Patients were excluded who had been hospitalized in the previous 4 months, had documented significant aortic stenosis or ejection fraction below 40%, sick-sinus syndrome, advanced heart block, or other significant comorbidity limiting life expectancy.

Intervention. Patients were randomized to 1 of 2 treatments: "usual care" ($n = 49$), with optimal adjustment of their usual antianginal medications (which could be short- and long-acting) or "once-a-day care" ($n = 51$), with conversion to a regimen consisting solely of long-acting agents (long-acting diltiazem ± nitroglycerin patches ± atenolol). According to the study algorithm, both groups underwent drug titration by a cardiovascular nurse practitioner to optimize angina control.

Main outcome measures. The primary outcome was 3-month change in Seattle Angina Questionnaire [1] scores, which quantify physical limitation resulting from CAD, angina stability over the preceding month, frequency of angina symptoms, satisfaction with treatment for CAD, and patients' perception of how coronary disease limits their quality of life. Scores on the SF-36 were a secondary measure.

Main results. Mean age of patients was 64.6 years in the usual-care group and 65.3 years in the once-a-day group. Six patients (2 from the usual-care group and 4 from the once-a-day group) dropped out of the study. Among the remaining patients, no differences in physical limitation scores were noted between treatment groups. Subjects who received long-acting medications showed improved symptom control (3-month improvement in anginal stability, 19.1 versus 5.6; $P = 0.02$; in angina frequency, 17.8 versus 5.5; $P = 0.006$), more treatment satisfaction (3-month improvement, 8.2 versus 3.0; $P = 0.057$), and better quality of life (3-month improvement, 11.2 versus 5.6; $P = 0.09$) compared with patients whose pre-trial medications were optimized. Improvement in symptom control was statistically significant. No significant adverse effects were reported.

Conclusion. Converting patients with chronic stable angina to long-acting antianginal medications resulted in improved symptom control, with a trend toward better treatment satisfaction and quality of life.

## Commentary

Spertus and colleagues emphasize that this trial was aimed at evaluating effectiveness rather than efficacy. In comparing 2 different strategies for optimizing antianginal medications, the authors did not require that usual-care patients already receiving long-acting agents be switched to short-acting equivalents. (Of the usual-care group, 84% were taking calcium channel blockers and 29% were taking β blockers). The study design, which included other conservative considerations (eg, small sample size, a 10-point difference in scores defined as a clinically significant change, the last functional status scores for dropouts considered as final assessments), may have biased results toward the null hypothesis and made achievement of statistical significance more difficult. The imbalance in treatment groups (resulting from randomization) posed another problem with similar effect, as patients in the usual-care group showed lower angina frequency ($P = 0.053$). These limitations and potential biases were acknowledged in the authors' analysis, which provides reassurance of the validity of study results.

Two important variables—cost and patient compliance—are not considered in this study. However, the authors' data

partially support the assertion that once-daily antianginal agents improve treatment compliance and possibly response in addition to conferring benefits derived from different pharmacokinetics. Because of this advantage, clinicians may feel the need to switch patients to these more expensive drugs. Future research, perhaps with a larger sample size and in a less selected population (ie, non-VA setting), would likely provide more applicable data.

## Applications for Clinical Practice

For patients with stable angina, symptom control can be achieved by optimizing treatment with either short- or long-acting medications. Use of once-daily β blockers, calcium channel blockers, and nitrates seems to produce better angina control and possibly better treatment satisfaction and quality of life. However, the increased cost of these medications should be considered in the decision-making process.

## References

1. Spertus JA, Winder JA, Dewhurst TA, et al. Development and evaluation of the Seattle Angina Questionnaire: a new functional status measure for coronary artery disease. J Am Coll Cardiol 1995;25:333–41.