Medical Therapy Versus Coronary Angioplasty in Stable Coronary Artery Disease: A Critical Review of the Literature

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The recent publication of the Atorvastatin Versus Revascularization Treatment (AVERT) trial has renewed debate on the optimal management strategy for relatively stable patients with coronary artery disease. Currently, coronary angiography and percutaneous coronary intervention are often performed in stable patients with good exercise tolerance who have not been treated with proven medications such as aspirin, statins and beta-adrenergic blocking agents in conjunction with comprehensive lifestyle modification. We review the results of prior trials comparing medical therapy with angioplasty and assess their strengths and limitations and then make conclusions about the aggregate data. Next, we describe the ongoing Clinical Outcome Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial, which will be the largest of the studies comparing optimal medical therapy and percutaneous revascularization. This study will employ intensive medical management in all patients with coronary disease, and the incremental benefit of state of the art revascularization techniques in terms of clinical event reduction, quality of life issues and cost-effectiveness will be addressed. For now, aggressive medical therapy and revascularization should be viewed as complementary rather than opposing strategies. All patients with coronary heart disease should receive proven medical and lifestyle prescriptions to favorably alter the atherosclerotic process. Percutaneous revascularization without comprehensive risk factor modification is a suboptimal therapeutic strategy. (J Am Coll Cardiol 2000;36: 668–73) © 2000 by the American College of Cardiology

The results of the AVERT trial have rekindled the debate concerning the preferred therapeutic strategy in patients with stable single- or double-vessel coronary artery disease (CAD) (1). Consensus currently exists that coronary artery bypass grafting (CABG) is the treatment of choice for patients with significant obstruction of the left main coronary artery, as well as for those with triple-vessel disease and diminished left ventricular systolic function. In patients with stable CAD, percutaneous transluminal coronary angioplasty (PTCA) has generally been recommended for: 1) severe proximal stenoses where a large portion of myocardium is at risk, that is, proximal left anterior descending coronary artery (LAD) lesions; 2) coronary stenoses producing significant inducible ischemia on provocative testing; and 3) treatment for angina inadequately controlled with medical therapy. However, some interventional cardiologists often dilate significant coronary stenoses whether or not they are causing symptoms or producing evidence of ischemia on provocative testing. The reason for this broader utilization of PTCA is the belief that the more obstructive a plaque is, the more frequently it progresses to coronary occlusion (2).

Does the literature support mechanical revascularization of coronary stenoses in the absence of significant inducible ischemia? Our clinical practices and interpretation of previous studies should be consistent with our current understanding of the pathophysiology of unstable coronary syndromes. Coronary atherosclerosis initially manifests itself as endothelial dysfunction. In the presence of hypercholesterolemia or other risk factors, a dysfunctional coronary endothelium promotes thrombosis, inflammation and an increase in vasomotor tone (3). Acute coronary events such as myocardial infarction (MI) occur as a result of plaque disruption or ulceration with subsequent thrombosis. Most “vulnerable” plaques are nonobstructive (that is, less than 50% of the vessel lumen) in nature. In addition, several large clinical trials have shown that a 30% reduction of low-density lipoprotein cholesterol (LDL-C) results in approximately a 30% reduction in the incidence of major coronary events (4). This benefit may largely be explained by the transformation of unstable plaques into ones less prone to rupture.

Do the results of the AVERT trial provide us with new support for this theory? Should our current practice patterns change based on these results? In this report, we reviewed five studies that compared medical management to PTCA in the treatment of stable coronary artery disease (Table 1). We then critically examined the AVERT trial in detail and evaluated how these results should impact clinical practice.

ANGIOPLASTY COMPARED TO MEDICINE (ACME)

The ACME trial involved 212 patients randomly assigned to PTCA or medical therapy (5). The subjects had stable angina, a positive exercise stress test (defined as ST segment
depression of ≥3 mm) or an MI within the three months preceding enrollment. In addition, cardiac catheterization revealed a 70 to 99% stenosis in the proximal two-thirds of one major epicardial coronary artery or similar serial stenoses confined to the proximal two-thirds of the same artery or its branches. The subjects then underwent a baseline exercise stress thallium test. If the stress test results were positive for ischemia (defined as ≥1 mm of horizontal or downsloping ST depression or the presence of angina with a reperfusion defect on thallium scan), then randomization took place. Medical therapy consisted of a stepped-care approach using nitrates, beta-adrenergic blocking agents, calcium channel blockers or a combination of these drugs, with the goal of eliminating angina. All patients received a full strength aspirin (325 mg) daily. Six months after randomization, all patients underwent repeat stress testing and angiography. The major end points of the study included changes in exercise tolerance and anginal frequency.

Compared with medically treated patients, those who underwent PTCA had significantly better exercise duration and time to onset of angina, fewer anginal episodes per month, improved thallium myocardial perfusion scores as well as better psychological well-being scores. At the same time, PTCA treated patients underwent more bypass surgeries (7 vs. 0, p < 0.01) and suffered a similar number of MI’s (5 vs. 3, p = NS) and deaths (0 vs. 1, p = NS). As seen in this study, the incidence of death or MI is very low in patients with single-vessel CAD. The authors concluded that the value of PTCA in terms of improved exercise tolerance without angina and a reduced need for antianginal medication should be weighed against the inherent risks and greater initial costs of the procedure (5).

The same investigators conducted a pilot study of PTCA versus medical therapy in 101 patients with double-vessel CAD (6). The eligibility criteria, outcomes assessed and study protocol were the same as that in the ACME trial, but follow-up was generally longer. Both the PTCA and medically treated groups had comparable improvement in exercise duration, time to onset of angina, frequency of angina, thallium perfusion scores and quality of life scores at six months compared with baseline. The two treatment arms also did not differ in the number of deaths and MIs. The investigators’ explanation for the lack of apparent benefit of PTCA in these patients was that the likelihood of complete revascularization decreased as the number of diseased vessels increased; moreover, the chance of restenosis increased as the number of dilated vessels increased (6).

### Table 1. Trials of Medical Therapy vs. Revascularization

<table>
<thead>
<tr>
<th>Study</th>
<th>Type of Participant</th>
<th>Study Design</th>
<th>Major Findings</th>
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<tbody>
<tr>
<td>ACME 1992</td>
<td>n = 212, 1 vessel CAD</td>
<td>Medical Rx vs. PTCA</td>
<td>PTCA improved exercise tolerance &amp; reduced need for antianginal medications with no decrease in clinical events</td>
</tr>
<tr>
<td>ACME-2 1997</td>
<td>n = 101, 2 vessel CAD</td>
<td>Medical Rx vs. PTCA</td>
<td>No benefit of PTCA over medical arm</td>
</tr>
<tr>
<td>ACIP 1995</td>
<td>n = 558 with ischemia suitable for revascularization</td>
<td>Medical Rx (anginal-guided vs. ischemia guided) vs. revascularization</td>
<td>Revascularization produced better event-free survival</td>
</tr>
<tr>
<td>MASS 1995</td>
<td>n = 214; proximal LAD stenosis</td>
<td>Medical Rx vs. PTCA vs. CABG</td>
<td>CAGB arm had better event–free survival</td>
</tr>
<tr>
<td>RITA-2 1999</td>
<td>n = 1,018; 1 to 2 vessel disease</td>
<td>Medical Rx vs. PTCA</td>
<td>PTCA arm had fewer MIs</td>
</tr>
<tr>
<td>AVERT 1999</td>
<td>n = 341, 1 to 2 vessel disease</td>
<td>Medical Rx with high dose statin vs. PTCA</td>
<td>Strong trend for fewer events in medical arm</td>
</tr>
<tr>
<td>COURAGE</td>
<td>n = 3,260, 1 to 3 vessel disease, patients with angina</td>
<td>Aggressive medical therapy vs. aggressive medical therapy plus PTCA</td>
<td>(In progress)</td>
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ACIP = Asymptomatic Cardiac Ischemia Pilot trial; ACME = Angioplasty Compared to Medicine trials; ACME 2 = Angioplasty Compared to Medical Therapy in Two Vessel Disease; AVERT = Atorvastatin Versus Revascularization Treatment trial; CABG = coronary artery bypass grafting; CAD = coronary artery disease; COURAGE = Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation trial; LAD = left anterior descending coronary artery; MASS = Medicine, Angioplasty or Surgery Study trial; MI = myocardial infarction; PTCA = percutaneous transluminal coronary angioplasty; RITA-2 = Second Randomized Intervention Treatment of Angina trial.
There are several shortcomings with both of these studies. In the ACME trial, over 9,500 patients were initially screened, but only 4% met eligibility criteria. This fact brings into question the applicability of the study to everyday practice. Both trials enrolled small numbers of patients who sustained few clinical events; this reduced the power to detect significant differences in outcomes between treatment groups. Moreover, as seen in subsequent trials, ACME predated the widespread use of stents and glycoprotein IIb/IIIa inhibitors, which improve procedural outcomes. In addition, the medical therapy protocol did not mandate the use of lipid-lowering drugs, which have been consistently shown to favorably alter long-term prognosis.

ASYMPTOMATIC CARDIAC ISCHEMIA PILOT (ACIP)

The ACIP study enrolled 558 patients who were followed for a two-year time period (7,8). These patients were required to be clinically stable with angiographically proven CAD ($\geq 50\%$ stenosis in $\geq 1$ major vessel or branch) that was suitable for revascularization. In addition, subjects manifested ischemia during exercise or chemical stress testing and $\geq 1$ episode of asymptomatic ischemia during 48 h ambulatory ECG monitoring. The subjects were then randomized to one of three treatment strategies: 1) angina-guided medical treatment, 2) ischemia-guided medical treatment, or 3) revascularization (PTCA or CABG as deemed most appropriate by physicians at the clinical site). The medical therapy mandated by ACIP consisted of either atenolol $\pm$ nifedipine or diltiazem $\pm$ isosorbide dinitrate.

After two years, the mortality rate was $6.6\%$ for patients randomized to angina-guided therapy, $4.4\%$ for ischemia-guided therapy and $1.1\%$ for revascularization therapy ($p < 0.005$ between angina-guided and revascularization). The rates for death or nonfatal MI were $12.1\%$, $8.8\%$ and $4.7\%$ in the same three groups, respectively ($p < 0.01$ between the angina-guided and revascularization strategies). The rates of death, MI or recurrent hospitalization for cardiovascular events were $41.8\%$ for angina-guided treatment, $38.5\%$ for ischemia-guided treatment and $23.1\%$ for revascularization treatment ($p < 0.003$ between the invasive group and both medically treated groups). In addition, there was a $29\%$ rate for nonprotocol revascularization that was thought to be clinically indicated in both medically treated groups versus only $11\%$ with invasive treatment.

After one year, results of ambulatory ECG monitoring revealed that more patients had complete suppression of ischemia with revascularization ($31\%$ in angina-guided patients, $36\%$ in ischemia-guided patients and $57\%$ in invasively treated patients, $p < 0.001$ between revascularization and both medical arms). Exercise stress testing also demonstrated less exertion-related angina and ischemia in the PTCA/CABG arm (8). Subgroup analysis of all of the data suggested that the benefit of the revascularization strategy was concentrated in those with proximal LAD stenoses and, to a lesser extent, in those with three-vessel disease.

Results of the ACIP study led the authors to conclude that initial revascularization may substantially improve the two-year prognosis of patients with objective evidence of ischemia and suitable coronary anatomy, even if their angina was controlled on conservative medical therapy. Although this pilot study was not statistically powered to detect differences in major clinical outcomes, it is the only randomized trial to show a decrease in death and nonfatal MI with revascularization. Nevertheless, there were too few events to allow for an accurate measurement of effect size. In addition, the beneficial effects of medical therapy may have been underestimated because anti-ischemic medications were not titrated to maximal doses, an increase in dosages of blinded medications did not occur after 12 weeks, and aggressive lipid lowering was not mandated as part of the treatment.

MEDICINE, ANGIOPLASTY OR SURGERY STUDY (MASS)

The goal of the MASS was to determine the relative efficacies of medical treatment, PTCA or CABG with a mammary artery conduit in patients with stable angina and a single severe proximal stenosis of the LAD (9). The MASS was a randomized trial of 214 patients with a $\geq 80\%$ stenosis of the LAD before the first diagonal branch; average follow-up was $3.5 \pm 1.5$ years. All patients had Canadian Cardiovascular Society (CCS) class II angina or less. The primary end point was the combined incidence of cardiac death, MI or refractory angina requiring revascularization. Secondary outcomes included functional anginal class and treadmill stress test results at two years. The object of medical therapy was to eliminate angina, and it consisted of aspirin, nitrates, beta-blockers and calcium-channel blockers.

After three years of follow-up, the event-free survival rate was significantly greater for those patients who underwent CABG as compared with those assigned to PTCA (97% vs. 76%, $p < 0.01$) or medical treatment (97% vs. 83%, $p < 0.01$). Both revascularization strategies resulted in greater percentages of angina-free patients (98% in bypass patients, 82% in PTCA patients and 32% in medical patients), as well as freedom from ischemia during stress testing at two years (94%, 79% and 34%, respectively, $p = 0.01$ for medical therapy vs. both revascularization strategies). Progression of atherosclerosis to stenoses $\geq 50\%$ in vessels that previously did not have significant disease was seen in 35% of subjects, about equally divided among the three treatment arms.

While both invasive treatments resulted in greater symptomatic relief and less exercise-induced ischemia, the prognosis for patients with single-vessel disease and preserved left ventricular systolic function was good. There was a trend for fewer ischemic events in the medical therapy group than there was in the PTCA group. Coronary artery bypass grafting for critical proximal LAD disease resulted in superior event-free survival compared with medical therapy or PTCA. Most of this benefit consisted of a reduction in refractory angina requiring future revascularization. In all
three groups, MI-free survival was excellent. This study, like most of the other medical therapy versus intervention trials, was limited by its relatively small size, low number of major cardiovascular events, lack of use of newer interventional techniques and the absence of aggressive lipid lowering as an integral part of medical therapy.

**SECOND RANDOMIZED INTERVENTION TREATMENT OF ANGINA (RITA-2)**

The Coronary Angioplasty versus Medical Therapy for Angina: RITA-2 trial was a randomized, controlled, multicenter trial of 1,018 patients who were followed for a median of 2.7 years in the United Kingdom and Ireland (10). All patients were required to have an arteriographically proven significant stenosis (defined as a $\geq 50\%$ stenosis in at least two radiographic projections or a $\geq 70\%$ stenosis in one projection) in one to two major epicardial vessels that were amenable to PTCA. Subjects were randomly assigned to treatment with PTCA (504 patients) or medical therapy (514 patients); 40% of the patients had multivessel CAD. The primary end point was the combined frequency of death and nonfatal MI.

At the trial’s conclusion, 32 PTCA patients versus 17 patients managed medically suffered death or nonfatal MI (6.3% vs. 3.3%, $p = 0.02$). There were 21 nonfatal MI’s (4.2%) in the PTCA group versus 10 (2.0%) in the medically treated arm; this difference was largely explained by the seven procedure-related infarcts in the PTCA group. There was no mortality difference between the two groups (2.2% vs. 1.4%, $p = 0.02$). However, PTCA patients suffering from class II angina or worse at baseline appeared to benefit from their procedure with a 20% lower frequency of angina and a 1 min longer mean exercise time at six months, when compared with the medical group. This benefit diminished, however, over the course of the following two years.

These results show that the greater symptomatic improvement and better exercise performance in the PTCA group came at the expense of a higher risk of nonfatal MI. This increased risk was mainly due to procedure-related events, and most occurred within three months of randomization. The authors concluded that routine PTCA of a severe coronary stenosis does not reduce the risk of MI (10). The RITA-2 trial is the largest of these trials, and it found that PTCA improves anginal symptoms at the expense of a higher postprocedural event rate. Important limitations of the trial included the fact that stenting and glycoprotein IIb/IIIa inhibitors were not employed. In addition, medical therapy was also suboptimal since only 20% of patients were receiving triple-drug antanginal treatment, and lipid lowering therapy was not mandated.

**ATORVASTATIN VERSUS REVASCULARIZATION TREATMENT (AVERT)**

The AVERT study was designed to help resolve some of the questions left unanswered by these previous trials (1). This was an 18-month, open label, multicenter study of 341 patients who were randomized to receive aggressive lipid lowering therapy with atorvastatin 80 mg/day or PTCA followed by usual care (which could also include lipid-lowering therapy). Eligibility criteria included: an LDL-C $\geq 115$ mg/dl, triglycerides $\geq 500$ mg/dl, CCS class II or less angina, the ability to complete $\geq 4$ min of a Bruce protocol treadmill test or equivalent on a bicycle protocol, and a stenosis of $\geq 50\%$ in $\geq 1$ coronary artery.

The subjects were stratified based on the presence of single- or double-vessel disease. The primary outcome examined was the occurrence of ischemic events defined as cardiac death, cardiac arrest, nonfatal MI, stroke, CABG, percutaneous coronary intervention (PCI) or worsening angina requiring hospitalization. Secondary outcomes included the time to occurrence of the first ischemic event, change in angina class, incidence of worsening angina, changes in lipoproteins, quality of life and all-cause mortality.

The mean percentage diameter coronary artery stenosis in both groups was around 80%. Almost 75% of patients in the PTCA group received lipid-lowering therapy at some time during the study; however, it was at a much lower dose than the medically treated group. At least 95% of subjects were compliant with the medical regimen, and no one was lost to follow-up. At baseline, there were small but significant demographic and angiographic differences between the groups in gender, concurrent use of aspirin or other anticoagulants and the presence of LAD disease. In fact, there was a higher prevalence of LAD disease in the atorvastatin group. Separate analyses for each gender and for patients with and without LAD disease showed the trends within these subgroups to be similar to the overall results.

As expected, the atorvastatin group had significantly lower total cholesterol, LDL-C (77 vs. 119 mg/dl) and triglycerides than the PTCA group at the end of the trial. By the end of the trial, 71% of the PTCA group had been placed on a statin. Moreover, significantly more PTCA-treated patients had improvement in their angina class when compared with the medical cohort. The most interesting finding, however, related to the category of ischemic events, where atorvastatin patients had a 36% reduction versus the invasive arm (13% vs. 21%, $p = 0.048$). Due to two interim analyses, the significance level was adjusted from $p = 0.05$ to $p = 0.045$. The use of aggressive lipid lowering was associated with a significantly longer time to a first ischemic event ($p = 0.03$) with the major benefit of atorvastatin on event reduction occurring after six months. The study also demonstrated that the routine use of atorvastatin 80 mg/day was safe, with only four patients (2%) having significant liver function test abnormalities and no patients having marked elevation of creatine phosphokinase levels.

Based on the above findings, the investigators concluded that aggressive lipid lowering with a statin is at least as effective as PTCA/usual care in decreasing the number of ischemic events in stable patients with one- or two-vessel CAD. Furthermore, in patients with CCS class II or less
angina and relatively preserved left ventricular systolic function (ejection fraction ≥40%), an initial medical strategy including aggressive lipid lowering with a statin may reduce the likelihood of ischemic events and, thereby, delay or prevent the need for revascularization. In addition, the greater difference in the incidence of ischemic events after the first six months suggests that one major beneficial effect of lipid lowering is plaque stabilization. The greater separation of curves from months six through 12 probably reflects the development of fewer new lesions, slowed progression, as well as stabilization of existing coronary plaques and improved coronary endothelial function in the high dose statin group rather than an impact on the complications of restenosis, which would have been expected to be manifest in the first six months of the trial.

The results of this provocative study must be interpreted cautiously. Despite the use of many centers, only 341 subjects were enrolled in the study, while many thousands of eligible patients underwent elective PTCA at these hospitals. This indicates that the subjects were highly select patients. Any inherent bias in referring patients for inclusion into the trial at the individual sites may have been magnified due to the relatively small sample size.

While the study provides information regarding antianginal medication use for both groups at the beginning and end of the trial, there are no data relating to the dosages or the use of these medications at the 6 and 12 month points in the trial. Most importantly, the major difference between the PTCA and atorvastatin groups did not occur in the category of more serious events (coronary heart disease [CHD] death, nonfatal MI), for which there was only a small number, but in the “subjective” area of worsening angina with evidence of myocardial ischemia resulting in hospitalization (25 patients vs. 11 patients). More data would be helpful regarding the extent of beta-adrenergic blocking agents and other antianginal therapy use during the trial.

The decision to admit a patient to the hospital is certainly subject to many potential biases and will vary greatly from physician to physician. Patients who have undergone PTCA are usually more sensitized to the recurrence of even minor chest pain since they are told it may represent restenosis. This may have led to more frequent stress tests and more repeat angiograms in the PTCA group. Furthermore, patients who undergo PTCA are often advised to have routine stress tests six months after their revascularization procedure. This may have resulted in the discovery of more cases of “silent restenosis” or progression of other lesions in the PTCA group, leading to more angiograms and possibly more revascularization procedures for worsening disease. On the other hand, longer term follow-up may have demonstrated more impressive benefits for aggressive lipid lowering as compared with initial revascularization therapy with suboptimal risk factor management.

Implications of prior studies. A review of the currently available literature concerning the use of medical therapy versus PTCA in stable CAD allows us to draw five conclusions:

1) The prognosis for patients with single-vessel CAD and preserved left ventricular systolic function is generally good, and PTCA of a flow-limiting stenosis does not reduce the rate of subsequent MI or mortality.

2) Percutaneous transluminal coronary angioplasty results in superior symptomatic relief of angina and improved exercise tolerance compared with medical therapy.

3) The benefits of revascularization may possibly be greater in patients with a stenosis of the proximal LAD as the culprit lesion.

4) The benefits of PTCA may come at the expense of a higher risk of periprocedural complications.

5) All studies to date have significant deficiencies including: an inadequate definition or execution of optimal medical therapy, a lack of aggressive lipid lowering as a vital part of medical management (except for the AVERT trial) and few interventional procedures performed with state-of-the-art techniques (for example, stents, glycoprotein IIb/IIIa inhibitors, clopidrogel). Other problems with the previous studies are small sample sizes, inadequate lengths of follow-up and small numbers of serious cardiovascular events.

The data from these trials do cast serious doubt on the practice of employing PCI to dilate every “significant” stenosis found at the time of cardiac catheterization (the “oculo-stenotic reflex”) without evidence of inducible ischemia on an adequate medical regimen. Because of its ability to improve exercise tolerance, PCI may be the preferred treatment in patients for whom the capacity to exercise is especially important. The ability to exercise vigorously may be especially helpful in the management of overweight/obese patients or type II diabetics for whom exercise will help with weight loss and improved glycemic control.

No clinical trial to date has utilized optimal medical therapy (11). While the exact definition of what constitutes this therapy can be debated, it would surely include aspirin, beta-blockers, lipid lowering agents (to achieve an LDL ≤100 mg/dl) and probably angiotensin-converting enzyme inhibitors in diabetics or patients with impaired left ventricular systolic function. Based on the impressive results of the Heart Outcomes Prevention Evaluation study, angiotensin-converting enzyme inhibitors should also be considered in all patients with vascular disease and at least high normal blood pressures (12). In addition, optimal medical therapy should also include treatment of hypertension to <130/85 mm Hg, good glycemic control (glycohemoglobin <7.0%), smoking cessation, regular aerobic exercise, dietary modification and weight loss in appropriate patients (13,14).

While the AVERT trial employed 80 mg of atorvastatin, we do not know if a lower dose of this particular statin or another statin to reach an LDL-C <100 mg/dl would have been just as effective. The authors of AVERT do not state whether the majority of the PTCA group patients were on
statins during the first 12 months of the trial. Use of a lower dose of atorvastatin certainly costs considerably less and is associated with fewer significant increases in liver function tests and complaints of myalgias than the maximum dose of atorvastatin. The question of how far we should lower LDL-C in a secondary prevention setting will be answered by the Study of the Effectiveness of Additional Reductions in Cholesterol and Homocysteine study, which examines 12,000 post-MI patients randomized to either 20 mg or 80 mg of simvastatin and the Treating to New Targets trial, which compares 10 mg of atorvastatin (estimated to achieve a mean LDL-C of 100 mg/dl) with 80 mg of atorvastatin (estimated to achieve a mean LDL of 75 mg/dl) in CHD patients.

**CLINICAL OUTCOMES UTILIZING REVASCULARIZATION AND AGGRESSIVE DRUG EVALUATION (COURAGE)**

The important issues addressed in AVERT will be reevaluated in the ongoing COURAGE trial (15). Potential study participants must have objective evidence of myocardial ischemia, be eligible for PCI and have CCS class I to III angina; of note, 56/341 subjects in AVERT were asymptomatic. In this trial, all patients will be placed on an optimal medical regimen with aspirin, beta-blockers, statins and angiotensin-converting enzyme inhibitors, if indicated. Subjects will then be randomized to continue with aggressive medical therapy alone or to undergo percutaneous revascularization after the institution of aggressive medical therapy. This trial will enroll 3,260 patients, who will be followed for a mean of 4.5 years.

Due to its much larger sample size than the previous trials, COURAGE is the first randomized controlled trial comparing PCI and aggressive medical therapy in patients with one- to three-vessel CAD that will have the statistical power to assess the combined primary end point of nonfatal MI and total mortality. The study’s hypothesis is that state of the art PCI plus intensive medical therapy will be superior to intensive medical management alone. The projected cumulative three-year cardiac event rates are 11% and 14%. There will be 38 enrollment sites (12 Veterans Affairs hospitals, 13 non-Veterans Affairs hospitals and 13 Canadian hospitals). The COURAGE trial will also have a detailed quality of life and economic components to examine the cost-effectiveness of the coronary intervention.

**Summary.** Based on our current understanding of the pathophysiology behind unstable coronary syndromes, PTCA and medical therapy should be viewed as complementary, rather than opposing, strategies. Currently, only a minority of patients with CHD receive therapy proven to favorably alter the atherosclerotic process. While angioplasty improves coronary blood flow considerably more than lipid lowering does, its effects are restricted to the target vessel, and they may not be maintained over time without concomitant lipid lowering therapy (16). All CHD patients would benefit from comprehensive risk factor modification and judicious use of revascularization procedures. Before a relatively stable patient with angina is referred for PTCA, practitioners should employ the fundamental ABC’s of stable angina management: Aspirin and Antianginals, Beta-blockers and Blood pressure control, Cholesterol management and Cigarette cessation, Dietary improvements and Diabetes control, Education and Exercise (17).

**REFERENCES**