

MEDICAL THERAPY VERSUS PERCUTANEOUS CORONARY INTERVENTION AND STABLE CORONARY ARTERY DISEASE.

INTRODUCTION:

The decision to perform PCI (percutaneous coronary intervention) is complex. At the core, it depends on assessment of the risk versus benefit ratio in a given patient. There are approximately 500,000 PCI's performed in the United States each year. In patients with acute myocardial infarction (especially with ST segment elevation), there is good data to support myocardial salvage and even a significant mortality benefit of PCI. In unstable angina or medically refractory angina, the advantage of PCI is often clear. The decision in patients with stable angina is more complex. The most compelling reason to intervene would seem to be either: (1) Prevent morbidity (MI) or mortality or (2) Improve quality of life.

In acute coronary syndrome (MI or unstable angina), there is a high incidence of morbidity and a moderate incidence of mortality, so it is much easier to measure the effect of a given intervention on these "hard" end points. In chronic stable angina, the incidence of MI and death are fairly low, so it would take a large study over a long period of time to have enough statistical power to show clear benefit in these "hard" end points. Despite the large number of patients with stable angina who are treated with medical therapy and PCI each year, very few studies have even looked at a comparison of an interventional versus conservative strategy. There are six completed trials in the literature and all have had significant limitations. Below we will review the trials before trying to come to some conclusions.

THE TRIALS

ACME and ACME-2

The initial ACME (angioplasty compared to medicine) trial randomized 212 patients with 70-99% stenoses in a single vessel with exercise induced ischemia, who had either angina, or an MI in the preceding three months with stable symptoms. ACME-2 was a pilot study that randomized 101 patients with double vessel coronary artery disease to angioplasty versus medical therapy. Neither trial had a significantly different incidence of MI or death (these were not the major end points and the studies were too small).

The smaller ACME-2 trial showed no significant difference in the major end points which were exercise testing, angina, and quality of life scores, but it was a very small trial. The single vessel initial ACME did show a significant benefit to angioplasty in most end points. These included better exercise duration and time to onset of angina on stress testing, fewer anginal episodes per month, improved Thallium myocardial perfusion scores, as well as, better psychological well being scores. The PTCA group did, however, require more bypass surgeries. There were a number of short comings in these trials. The most obvious is small numbers of patients and the fact that of 9,500 initially screened patients, only 4% meet eligibility criteria.

ACIP (Asymptomatic Cardiac Ischemia Pilot Study)

This study had a complex design that included clinically stable patients with one to three vessel disease with ischemia on stress testing and asymptomatic ischemia during 48 hour ambulatory ECG monitoring. These patients were randomized to one of three groups: (1) Angina guided medical treatment, (2) ischemic guided medical treatment, or (3) revascularization (PTCA or CABG) as deemed most appropriate by physicians at the clinical site. After two years, though the mortality rate was higher in the medical therapy groups (6.6% angina guided, 4.4% ischemic guided, and 1.1% for PTCA/CABG). Also, the combined death and non-fatal MI rates were better for revascularization therapies (12.1%, 8.8%, 4.7%) for the same groups. Other end points of suppression of ischemia and angina were also better in the PTCA/CABG arm. The authors concluded that initial revascularization with PTCA or CABG improved the two year prognosis of patients with objective evidence of ischemia and suitable coronary anatomy even though their angina was controlled on medical therapy. The biggest benefit of revascularization (PTCA/CABG) strategy was in patients with proximal LAD disease. This study has limitations in that PTCA and CABG patients were combined in the same group and aggressive lipid therapy and aggressive dose titration of antianginals were not stressed.

MASS (Medicine, Angioplasty, or Surgery)

This is a small study of 214 patients with single vessel disease with a greater than or equal to 80% stenosis of the proximal LAD. The average followup was 3.5 plus or minus 1.5 years. The patients were randomized to CABG (LIMA to the LAD), PTCA, or medical therapy. Both CABG and PTCA resulted in greater angina relief and less exercise induced ischemia. However, in all these groups, MI free survival was low, but the event free survival rate was significantly lower in the CABG group and there was a statistically insignificant trend towards more non-fatal MI's in the PTCA group than the medical therapy group. This study was limited by small patient size, a low number of major events, lack of new interventional techniques (eg. stents or IIb, IIIa receptor blockers, and absence of aggressive lipid lowering in any group.

RITA II (Second Randomized Trial of Angina)

Second randomized trial of angina. This was a trial of 1,018 patients with one or two vessel disease randomized to PTCA versus medical therapy. The mortality rates were similar, but there was a higher incidence of non-fatal MI in the PTCA group versus medical therapy. There was greater symptomatic improvement and better exercise tolerance in the PTCA group. Important limitations were the lack of stenting and glycoprotein IIb/IIIa inhibitors. (Neither were used in this trial). Also, lipid lowering was again not mandated.

AVERT (Atorvastatin Versus Revascularization Treatment)

This recently completed trial randomized 341 patients with stable angina and one or two vessel disease felt to be a candidate for either PTCA or medical therapy including Atorvastatin at 80 mg. per day. The PTCA group could also receive lipid lowering therapy, but it was much less intense and less patients were treated. The major finding was reduced ischemic events in the intense Atorvastatin group (13% versus 21%) over 18 months. Interestingly, the major difference between the groups was after the first six months, suggesting it was mainly related to plaque stabilization, rather than procedural or restenosis effects that might occur in the first six months. Also, interesting was the fact that only 2% of the patients had significant liver function test abnormalities and none had marked CPK elevations with Atorvastatin at 80 mg. per day. Despite higher event rates over 18 months, more PTCA treated patients had improvement in angina class and exercise tolerance.

DISCUSSION:

All the trials to date are limited. There are limited numbers and often low selection numbers compared with patients screened. Most of the trials did not include maximal medical therapy, especially lipid lowering, with the exception of the AVERT trial. The PTCA arm did not reflect the state of the art PCI. Stenting and glycoprotein IIb/IIIa inhibitors which significantly improve both acute complications and longer term results, were not employed. An on-going trial should answer some of these limitations. COURAGE is a multicenter trial which will enroll 3,260 patients randomized to “state of the art” PCI plus aggressive medical therapy (including lipid lowering) versus aggressive medical therapy alone. This is basically an extension of the AVERT trial with significantly larger numbers and aggressive lipid lowering provided to the PCI group as well as to the medical therapy group.

CONCLUSIONS:

1. The decision of whether to perform PCI in stable angina patients remains complex and needs to be individualized with analysis of the goals and risks.
2. The prognosis for patients with preserved LV function, stable angina, and single vessel disease (especially if there are no high risk markers on non-invasive assessment) is good with either PCI or medical therapy.
3. PTCA results in greater symptom relief and better exercise tolerance than medical therapy. Also, psychological “well being” scores were better with PTCA.
4. PTCA (at least without stenting and use of glycoprotein IIb/IIIa inhibitors) of a flow limiting stenosis does not reduce the rate of subsequent MI or mortality. This is likely due to two factors: (a) peri-procedural complications and (b) most infarcts do not come from stable lesions, but rather plaque rupture of a previously non-critical stenosis.
5. Aggressive lipid lowering (and other risk factor modification) is more likely to prevent an MI than is PTCA. Aggressive lipid lowering and risk factor modification should be applied to all PCI patients as well.
6. A patient who has well controlled angina, and who is “happy” with medical therapy, and does not have high risk markers by non-invasive assessment, need not undergo PCI.
7. A patient who has stable symptoms, but is active and somewhat limited or feels compromised by medical therapy likely will benefit from PCI. Some patients also benefit psychologically from being “fixed” by PCI. This is an important factor in selected patients.
8. Future studies with more “state of the art” PCI (optimal stenting and appropriate use of glycoprotein IIb/IIIa inhibitors) and more optimal medical therapy in both PCI and “pure” medical therapy groups will be helpful in this decision.

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