REVIEW ARTICLE

COMPARISON OF EFFECTIVENESS OF PERCUTANEOUS CORONARY INTERVENTION AND MEDICATION IN PATIENTS WITH STABLE ANGINA

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ABSTRACT

Stable angina is one of the main manifestations of coronary artery disease. The presence of angina symptoms, a positive exercise test for myocardial ischaemia and confirmation of coronary artery atherosclerosis by coronary angiography are the bases of diagnosis of chronic stable angina. Present research however has yet not completely determined the helpfulness of invasive treatment of the coronary arteries with percutaneous coronary intervention in comparison with medication. Percutaneous coronary intervention is recognized to reduce the incidence of death and myocardial infarction in patients who suffer from acute coronary syndrome, the same benefit however does not appear to extend to patients who have stable coronary artery disease. Although some studies have shown improvement in survival for the patients with stable angina undergoing PCI but most have shown that PCI does not show any improvement in mortality or risk of myocardial infarction in these patients.

KEY WORDS: Percutaneous coronary intervention; Angina; Myocardial infarction.

INTRODUCTION

Now-a-days coronary artery disease (CAD) is a danger throughout the world while stable angina is one of the main manifestations of CAD.[1,2] The presence of angina symptoms, a positive exercise test for myocardial ischaemia, and confirmation of coronary artery atherosclerosis by coronary angiography are the bases of diagnosis of chronic stable angina.[3] The best possible management of such patients is the contentious problem in current years.[2,3] Present research however has yet not completely determined the helpfulness of invasive treatment of the coronary arteries with percutaneous coronary intervention (PCI) in comparison with medication. Percutaneous coronary intervention is recognized to reduce the incidence of death and myocardial infarction (MI) in patients who suffer from acute coronary syndrome, the same benefit does not appear to extend to patients who have stable coronary artery disease.[5,6] Because of ease of use of non-invasive methods of diagnosing coronary artery disease gradually increases, asymptomatic patients are often referred for percutaneous coronary intervention. However, a necessary condition for any preventive therapy is that

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it should fight against a danger i.e. which in the case of stable coronary artery disease is acute myocardial infarction and death. Taken together, data from three post-hoc COURAGE sub-studies suggest that higher risk patients with chronic stable angina benefit from PCI and as a result, may have subsequent reduction in hard clinical events, death or myocardial infarction. There are a number of studies regarding the matter under consideration which will be discussed below one by one.

DISCUSSION

ACME-1 trial (Angioplasty Compared to MEdicine) was one of the first studies to compare the efficacy of percutaneous coronary intervention with medicine alone in patients with stable angina.[7] In this study it was known that patients have one-vessel disease and a positive exercise test, and were followed for a total of six months. The researchers found greater improvement of symptoms and better exercise tolerance in the percutaneous coronary intervention group, but the incidence of death and myocardial infarction was similar in the two groups however percutaneous coronary intervention group was associated with a greater cost and a higher complication rate. ACME-2 trial studied patients having two-vessel disease, stable angina, and a positive stress test, who were treated with either percutaneous coronary intervention or medication and the outcome were compared with those from the previous study of patients with one-vessel disease[8]. The study showed that angioplasty was less

effective in controlling symptoms in patients with two-vessel disease and stable angina than in those with one-vessel disease.

The ACIP (Asymptomatic Cardiac Ischaemia Pilot) studies those patients were included who were either without symptoms or had symptoms controlled with medication, with asymptomatic ischaemia on 24-hour Holter monitoring and a positive exercise test[9,10]. The study showed, over a two-year follow up, that these patients had a better prognosis when they were reperfused either with angioplasty or surgically. The AVERT trial (Atorvastatin Versus Revascularisation Treatment)was especially designed to observe the outcome of aggressive lipid-lowering treatment on the incidence of ischaemic symptoms.[11] The study enrolled341 patients with mild to moderate stable angina and good left ventricular contractility, who were followed for 18 months and were treated either with angioplasty or with medication the latter included 80 mg atorvastatin per day. The findings of the study showed that medication achieved a reduction in anginal complaints similar to that achieved by angioplasty. ASS study (Medicine, Angioplasty, or Surgery Study) was the type of study which is also called as MASS study, 214 patients of stable angina having first-rate left ventricular function, with >80% stenosis of the proximal anterior descending coronary artery branch, were followed for about 5 years.[12] The patients were treated with either angioplasty or medicines, even though angina episodes were reduced in the PCI group but there was no difference in the "hard" endpoints such as myocardial infarction and death.

ALKK study (ArbeitsgemeinschaftLeitendeKardiologischeKrankenhausärzte)[13] was about 300 patients who were enrolled with mild or no angina after a recent myocardial infarction (one to six weeks in the past) and one vessel disease, who were followed for 56 months. In these stable patients it was shown that PCI in the offender artery was linked with a lower use of nitrates and a better prediction.RITA-2 trial (Second Randomised Intervention Treatment of Angina) was about 1018 patients without angina who had angiographically documented coronary artery disease were at first treated with only medication or PCI.[14,15] Over a seven-year follow up, the PCI group had fewer anginal episodes and better exercise tolerance, but there was no reduction in acute infarctions or death. In this study however it was a fact that almost 35.4% of the patients in the medication group in due course undergo reperfusion during the study period. The TIME study (Trial of Invasive versus Medical therapy in the Elderly) included patients having age more than 75 years who had angina that was refractory to at least two anti-anginal drugs.[16-19] The aim of the study was to investigate the effect of medication alone, or in combination with PCI, in reducing major adverse cardiovascular events (death, non-fatal myocardial infarction, hospitalisation for angina with or without reperfusion) and improving the patients' quality of life, over a six-month follow up. The study demonstrated a small early improvement in quality of life in the group who underwent PCI. This study was followed for four years and there was no difference in mortality between the two groups. Therefore, invasive treatment could be used in elderly patients with refractory angina in order to relieve their symptoms, without promising any prolongation of life. Hambrecht et al studied 101 patients with stable one-vessel coronary artery disease (angiographic stenosis >75%), who were either treated with PCI or followed an exercise regimen (20 min daily on a bicycle ergometer).[20] The patients also had angina (Canadian Cardiovascular Society, CCS class I to III) and myocardial ischaemia documented by a non-invasive test. In this study it was found that patients who exercised showed a clinical improvement by one CCS class in comparison with the PCI group, as well as a longer interval free of cardiac events, at half the cost.

A sub-analysis of the DANAMI study (Danish Acute Myocardial Infarction study) included 1008 patients who had undergone thrombolysis because of an acute myocardial infarction and had residual ischaemia (silent or symptomatic), showed that invasive treatment reduced the risk of non-fatal reinfarction, as well as hospital admissions for unstable angina.[21] The INSPIRE (adenosine sestamibi SPECT Post- Infarction Evaluation)study followed 205 stable patients after acute myocardial infarction, with ejection fraction >35% and with high-risk criteria on myocardial adenosine scintigraphy (adenosine SPECT).[22] The aim of the study was to investigate the possible benefit of intensive drug therapy compared with PCI as regards the reduction in scintigraphically monitored ischaemia. It was found that optimal drug treatment had results comparable with those of reperfusion as regards the reduction in scintigraphic perfusion defect.

In the MASS II study about 611 patients with stable angina on a substrate of multi-vessel coronary artery disease (>70% stenosis in proximal segments of the coronary arteries) and documented myocardial ischaemia on exercise testing were treated either with medication alone or with PCI.[23-26] A comparison of the groups revealed no difference in cardiac deaths or total mortality. However, the PCI group had a significantly lower incidence of anginal episodes. The SWISSI II (SWiss International Study on Silent Ischemia)trial included 201 patients with a recent myocardial infarction and silent ischaemia.[27]The patients were treated either with medication alone or with PCI and were followed for a mean period ofabout ten years. The PCI arm showed a benefit in terms of reduced cardiovascular events.

COURAGE study (Clinical Outcomes Utilising Revascularisation and Aggressive Drug Evaluation).[28] had the period from 1999 to 2004 and numbers of patients were included about 2287 with stable angina and objective evidence of myocardial ischaemia,

who were treated with medication either alone or in conjunction with PCI. In this study the numbers of woman patients were very limited which were 15% of the total numbers and this was the limitations of this study. Patients with left main disease, a strongly positive exercise test, refractory angina CCS class IV, drug refractory heart failure or cardiogenic shock, or an ejection fraction <30% were excluded, as were those who had undergone reperfusion during the previous six months or who had a coronary anatomy unsuitable for PCI. The patients in this study had either >70% stenosis in the proximal segment of an epicardial coronary artery together with findings of

Myocardial ischaemia on exercise testing or the resting ECG, or >80% stenosis and typical angina. However, one quarter of the patients did not have angina symptoms. The mean follow up was 4.6 years. Anginain the medication group improved at one year, with a further benefit at five years. Although angina improved more in the PCI group initially, the difference was not statistically significant after five years. It should be taken into consideration that by the end of the study about a third of the patients in the medication group had undergone reperfusion because of treatment-refractory angina or because of a worsening of ischaemia on a non-invasive ischaemia test. In the COURAGE study, drug-eluting stents were implanted in only 2.7% of the patients. Finally, the study showed that there was no reduction in mortality in-patients treated with PCI, while the benefit in terms of symptom relief in the PCI arm was blunted with the passage of time.

Many investigators including Weintraub found that patients with stableangina who were treated with angioplasty showed a better state of health as determined by special questionnaires.[29]However, this small difference did not persist beyond 36 months. Gu et al studied 80 patients with stable angina and angiographically documented multi-vessel coronary arterydisease,[30,31] of whom were treated with PCI and with medication alone. No benefit was seen in terms of major cardiovascular events in either group.

Sub group study of COURAGE studied the selected patients from COURAGE who were evaluated in serial myocardial perfusion tests with the use of myocardial perfusion single photon emission computed tomography (MPS), the addition of PCI to drug treatment resulted in a further reduction in imaging-documented ischaemia; in particular, the benefit was greater in those with a bigger initial ischaemic burden.[32] A Japanese study of patients with stable angina and chronic low-risk coronary artery disease showed that the combination of PCI with medication reduced cardiovascular events over a 3.3-year follow up to a greater degree than medication alone.[32] In a meta-analysis of 17 studies of patients with stable coronary artery disease, it was found that a strategy of PCI therapy improved expected survival in comparison with medication.[33]

The recent BARI 2D study[33] **(**Bypass Angioplasty Revascularisation Investigation**)** was not able to show a benefit from PCI in terms of mortality and cardiovascular events in diabetic patients with chronic coronary artery disease and angina (>70% stenosis of a major coronary artery, or >50% stenosis and a positive exercise test), confirming and reinforcing the results of the COURAGE trial.[28]

Finally, a recent meta-analysis by Trikalinosetel[31] of all the studies from the last 20 years concerning the treatment of chronic coronary artery disease with PCI showed that, in a total of 25,388 patients, despite the technological advances, PCI did not reduce the incidence of fatal myocardial infarction or death compared to drug treatment alone.

CONCLUSION

Although some studies have shown improvement in survival for the patients with stable angina undergoing PCI but most of the studies and meta-analyses have shown that PCI of the coronary arteries does not show any improvement in mortality or risk of myocardial infarction in these patients.

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