Stable angina results from imbalance between myocardial oxygen supply and demand or a combination of both (figure 1).

However the commonest cause of stable angina is atherosclerotic narrowing of the affected artery usually more than 70% (Figure 2a). So long as the intima remains intact, the angina is stable but the moment intima gets disrupted there is superimposed thrombus formation resulting in acute occlusion of the affected artery which culminates in acute coronary syndrome. (Figure 2b).

The strategies for management of stable angina are outlined in figure 3.

However the most burning issue in stable angina is the optimum selection of a modality for its treatment, i.e. Medical management, percutaneous coronary interventions (PCI) coronary artery bypass grafting (CABG). The key questions in stable angina are:

1. Will the patients of stable angina on optimal medical treatment benefit from PCI in terms of death from any cause, myocardial infarction, stroke and hospitalization for ACS?
2. Will PCI produce quick relief of angina and provide quality of life benefit?
3. Can patients of three vessel disease with or without left main stem disease can be treated by PCI or CABG is the only option for this subset of patients?
4. If they can be treated by PCI, how to discriminate which patient will be better off with PCI and which patient with CABG?
5. If the anatomy of coronary arteries is feasible for both PCI and CABG. How to select the modality of revascularization?
6. What is the incidence of stroke with each modality and what is the incidence of graft occlusion and stent occlusion?

Several trials have been conducted to address this issue but the two landmark trials which are most often talked about are the

**STABLE ANGINA : LESSONS LEARNT FROM RECENT TRIALS**

**PC Manoria, Pankaj Manoria, Piyush Manoria, SK Parashar, RK Shrivastava, Bhopal**

Fig. 1

Fig. 2a : Stable Angina

Fig. 2b : Acute Coronary syndrome

Fig. 3
Calculated with the use of the chi-square test. Relative risks were calculated from the binary rates. P values were reported for PCI (relative risk, 2.29; 95% CI, 1.67 to 3.14), as was the overall rate of repeat revascularization (Panel C); and the composite primary end point of major adverse cardiac or cerebrovascular events (Panel D). The two groups had similar rates of death from any cause (relative risk with PCI vs CABG, 1.24; 95% confidence interval [CI], 0.78 to 1.98) and rates of death from any cause, stroke, or MI (relative risk with PCI vs. CABG, 0.90; 95% CI, 0.72 to 1.38). In contrast, the rate of repeat revascularization was significantly increased with PCI (relative risk, 2.29; 95% CI, 1.67 to 3.14), as was the overall rate of major adverse cardiac or cerebrovascular events (relative risk, 1.44; 95% CI, 1.15 to 1.81). The I bars indicate 1.5 SE. Relative risks were calculated from the binary rates. P values were calculated with the use of the chi-square test.

**COURAGE trial and SYNTAX trial.**

**COURAGE trial:***

In this trial, the patients were randomized to optimal medical therapy alone (n = 1,138) or PCI in addition to optimal medical therapy (OMT) (n = 1,149). OMT included antiplatelet therapy with aspirin (81-325 mg/day), or clopidogrel (75 mg/day) in aspirin intolerant patients in the medical therapy group and aspirin plus clopidogrel in the PCI group. All patients also received aggressive lipid-lowering therapy to a target low density lipoprotein (LDL) of 60-85 mg/dl. Anti-ischemic therapy included long-acting metoprolol, amiodipin, and isosorbide monitrate, alone or in combination, and either lisinopril or losartan as secondary prevention.

**Principal Findings:**

The large majority of patients (95%) had objective evidence of myocardial ischemia. Multivessel disease was present in 69% of patients, with only 31% having single-vessel disease. One-third of patients had proximal disease of the left anterior descending artery (LAD). Canadian Cardiovascular Society (CCS) class II or III angina was present in 58% of patients at study entry.

PCI was performed in 94% of the PCI cohort, with successful PCI in 93%. Optimal medication use during the study was high in both treatment groups, with use at 5 years of angiotensin-converting enzyme inhibitors in 64% of patients, statins in 93%, aspirin in 95%, and beta-blockers in 85%. LDL levels were reduced to a median of 71 mg/dl. Diet, exercise, and smoking cessation were also high in both groups.

The primary endpoint of death or MI did not differ for the PCI group compared with the medical therapy group (19.0% for PCI vs. 18.5% for medical therapy, hazard ratio [HR] 1.05, 95% confidence interval [CI] 0.87-1.27, p = 0.62). There was also no difference between PCI and medical therapy in the secondary composite endpoint of death, MI, or stroke (20.0% for PCI vs. 19.5% for medical therapy, HR 1.05, 95% CI 0.87-1.27, p = 0.62) or in the secondary endpoint of hospitalization for ACS (12.4% for PCI vs. 11.8% for medical therapy, HR 1.07, 95% CI 0.84-1.37, p = 0.56). Components of the composite endpoints did not differ between groups, including death (7.6% for PCI vs. 8.3% for medical therapy, HR 0.87, p = 0.38), nonfatal MI (13.2% vs. 12.3% HR 1.13, p = 0.33), or stroke (2.1% for PCI vs. 1.8% for medical therapy, p = 0.19) (figure-4).

Angina was significantly reduced in both groups during follow-up with no difference in the reduction between PCI and medical therapy at 5 years (freedom from angina in 74% of the PCI group and 72% of the medical therapy group, p = 0.35) but slightly higher rates of freedom from angina at the early time frame with PCI (at 1 year: 66% for PCI vs. 58% for medical therapy, p < 0.001; at 3 years: 72% for PCI vs. 67% for medical therapy, p = 0.02)

**Interpretation:**

Among patients with stable coronary artery disease, treatment with PCI was not associated with a difference in death or MI compared with treatment with medical therapy through 5 year of follow-up.

Despite patients in the study having stable angina, disease severity was relatively intensive, with the majority of patients having multi-vessel disease and objective evidence of ischemia at study entry, there were no differences in any of the clinical endpoints between the PCI and medical therapy groups, nor was there any treatment interaction with the pre-specified subgroups. Freedom from angina occurred slightly more frequently with PCI early in the trial but did not differ between the PCI and medical therapy groups by 5 years, with both arms showing marked reductions in angina throughout the trial.

The findings from the present study apply to stable angina patients and cannot be extrapolate to the acute coronary syndrome population, which has different pathophysologic characteristics, although the majority of patients currently undergoing PCI are for stable angina. While the majority of the PCI group did not receive drug eluting stents since most of the enrollment was completed prior to the introduction of these stents, there is no reason to
Stable Angina: Lessons Learnt from Recent Trials

**RESULTS**

Most of the preoperative characteristics were similar in the two groups. The rates of major adverse cardiac or cerebrovascular events at 12 months were significantly higher in the PCI group (17.8%, vs. 12.4% for CABG; P=0.002), in large part because of an increased rate of repeat revascularization (13.5% vs. 5.9%, P<0.001); as a result, the criterion for non inferiority was not met. At 12 months, the rates of death and myocardial infarction were similar between the two groups; stroke was significantly more likely to occur with CABG (2.2% vs. 0.6% with PCI; O=0.003) (figure-5).

**CONCLUSIONS**

CABG remains the standard of care for patients with three vessel or left main coronary artery disease, since the use of CABG, as compared with PCI resulted in lower rates of the combined end point of major adverse cardiac or cerebrovascular events at 1 year.

Both the trials have answered several questions pertaining to stable angina.

1. Will the patients of stable angina on optimal medical treatment benefit from PCI in terms of death from any cause, myocardial infarction, stroke and hospitalization for ACS?

The COURAGE trial showed no difference between the PCI group and medical therapy group in the composite of death myocardial infarction, and stroke (20.0%vs. 19.5%; hazard ratio, 1.05; 95% CI, 0.87 to 1.27; P=0.62); hospitalization for acute coronary syndrome (12.4% vs. 11.8%; hazard ratio, 1.07; 95% CI, 0.84 to 1.37; P=0.56); or myocardial infarction (13.2% vs. 12.3%; hazard ratio, 1.13; 95% CI, 0.089 to 1.43; P=0.33). This is understandable because the coronary lesions which produce myocardial infarction and death are the vulnerable plaques which are small and haemodynamically insignificant and are therefore obviously not touched by PCI.

However the courage trial has several limitations. Firstly the trial excluded patients with large area of myocardium at jeopardy and LAD lesion was present only in one third of cases. Secondly there was a high switch over rate from OMT group to PCI group. Thirdly the drug eluting stents (not available at that time) which decreases restenosis and contribute to better angina control were not used.

2. Will PCI produce quick relief of angina and provide quality of life benefit?

The courage trial showed that there were slightly higher rates of freedom from angina in the early time frame with PCI (at 1 year: 66% for PCI vs. 58% for medical therapy, P<0.001; at 3 years: 72% for PCI vs. 67% for medical therapy, P=0.02). However other trials have shown better relief of angina with PCI. There was no difference in this at the end five years (freedom from angina in 74% of the PCI group and 72% of the medical therapy group, P=0.35). The Seattle Angina Questionnaire (SAQ) which were similar at baseline in each treatment groups, the scores were higher in the PCI.
plus medical therapy than the medical therapy only group for 6 to 24 months. But these differences dissipated by 3 years. Further analysis showed that a greater proportion of patients treated with PCI than with optimal medical therapy alone had clinically significant improvements in scores for physical function, angina frequency, and quality of life for the first 6 months but these differences were no longer significant by 12 months.

3. Can patients of three vessel disease with or without left main stem disease be treated by PCI or CABG is the only option for this subset of patients?

The syntax trial showed that in patients of three vessels disease with or without left main stem disease and similar preoperative characteristics, the rates of major adverse cardiac or cerebrovascular events at 12 months were significantly higher in the PCI group (17.8%, vs. 12.4% for CABG; P=0.002), in large part because of an increased rate of repeat revascularization (13.5% vs. 5.9%, P<0.001); as a result, the criterion for non inferiority was not met. At 12 months, the rates of death and myocardial infarction were similar between the two groups. Despite the trial being negative in terms of primary end point, the trial clearly showed that patients of above subset can also be adequately treated by PCI with the only disadvantage of higher rate of repeat revascularization.

4. If they can be treated by PCI, how to discriminate which patient will be better off with PCI and which patient with CABG?

The SYNTAX trial clearly showed that patients with low SYNTAX scores (0 to 22) or intermediate SYNTAX scores (23 to 32) can be treated by either by PCI or CABG and the 12 months event rates were similar between the two treatment groups. Among patients with high SYNTAX scores (≥33, indicating the most complex disease), those in the PCI group had a significantly higher event rate at 12 months than those in the CABG group. Thus the message is patients with lower SYNTAX score rates < 32 can be treated either by PCI or CABG but patients with SYNTAX score > 32 should be treated only by CABG.

5. If the anatomy of coronary arteries is feasible for both PCI and CABG. How to select the modality of revascularization?

In this subset the decision is based on cost issues (more with PCI), quality of life (better with PCI), willingness to achieve repeat revascularization and motivation to accept surgery. Other factors like compliance of the patient for taking dual antiplatelet therapy, ischemic vs. bleeding risk and requirement of non-cardiac surgery in future, co-morbidities. etc. are also taken in consideration.

c. What is the incidence of stroke with each modality and what is the incidence of graft occlusion and stent occlusion.

The incidence of stroke was significantly higher with CABG (2.2% vs. 0.6% with PCI; P=0.003) than PCI. Majority of CABG in this trial were done on pump and this could have increased the stroke rate. In off pump surgery since aorta is not touched, there is minimal risk of stroke. The rates of symptomatic bypass graft occlusion and stent occlusion were same with PCI and CABG i.e. 3.5% but they have very different clinical consequences. Stent occlusion has high mortality and MI rates while the prognosis of bypass graft occlusion is less sinister but this is not amenable to thrombolysis.

REFERENCES