

# Healthy Heart

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**Honorary Editor :**  
Dr. Vipul Kapoor



## From the Desk of Hon. Editor:

Unprotected Left Main CAD (ULMCAD) has a varied spectrum of presentation. It can have a totally benign or indolent natural history or can be extremely malignant with the dreaded presentation of sudden cardiac death. Until recently patients with significant LM disease had only one treatment option viz CABG. But of late with advancements in technology and upgradation of Interventional skills an increasing number of such patients are presently undergoing successful Percutaneous Coronary Intervention (PCI) with comparable short, intermediate and long term result to CABG. This review attempts to highlight the indications, techniques and treatment modalities for left main CAD (LMCAD)

## LEFT MAIN CAD (PART - 1)

### INTRODUCTION :

Significant (defined as a greater than 50 percent angiographic narrowing) left main coronary artery disease (LMCAD) is found in 4 to 6 percent of all patients who undergo coronary arteriography. It is associated with multivessel coronary artery disease about 70 percent of the time.

This topic will discuss most aspects of the management of patients with LMCAD.

### DIAGNOSIS :

The diagnosis of left main coronary artery disease is usually made by coronary angiography.

Certain findings on exercise testing or, in patients with acute coronary syndromes on the electrocardiogram (ECG), are suggestive of left main coronary artery disease. These include diffuse and severe ST-segment deviation or significant ventricular arrhythmias on ECG monitoring or hypotension during exercise.

### PREVENTIVE THERAPIES :

All patients with left main coronary artery disease should receive preventive therapies known to decrease the risk of cardiovascular events, such as smoking cessation, achieving target blood pressure

goals, lipid lowering therapy with statins, exercise, and proper management of diabetes.

### SIGNIFICANT LEFT MAIN DISEASE:

Coronary artery bypass graft surgery (CABG) with optimal preventive therapies is preferred to optimal preventive therapies alone for all patients with significant left main coronary artery disease (LMCAD). CABG significantly improves survival.

Most patients with significant LMCAD are symptomatic and at high risk of cardiovascular events, since occlusion of this vessel compromises flow to at least 75 percent of the left ventricle, unless it is protected by collateral flow or a patent bypass graft to either the left anterior descending coronary artery or circumflex artery. Without revascularization, three-year survival is as low as 37 percent. CABG, when directly compared with medical therapy, is associated with significantly better cardiovascular outcomes, including mortality. In the Veterans Administration Cooperative Study performed in the 1970s, which compared a strategy of initial CABG versus deferred CABG, there was a substantial survival advantage for patients assigned to initial CABG at two years (93

#### Cardiologists

Dr. Satya Gupta (M) +91-99250 45780	Dr. Milan Chag (M) +91-98240 22107
Dr. Vineet Sankhla (M) +91-99250 15056	Dr. Urmil Shah (M) +91-98250 66939
Dr. Vipul Kapoor (M) +91-98240 99848	Dr. Hemang Baxi (M) +91-98250 30111
Dr. Tejas V. Patel (M) +91-89403 05130	Dr. Anish Chandarana (M) +91-98250 96922
Dr. Guntant Patel (M) +91-98240 61266	Dr. Ajay Naik (M) +91-98250 82666
Dr. Keyur Parikh (M) +91-98250 26999	

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Dr. Divyesh Sadadiwala (M) +91-8238339980	

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Dr. Vineet Sankhla (M) +91-99250 15056

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Dr. Amit Chitaliya (M) +91-90999 87400
--

versus 71 percent) and at 11 years, but not at 18 years. The benefit was greatest in high-risk patients with greater than 75 percent left main stenosis and/or left ventricular dysfunction; there was a nonsignificant trend toward benefit in patients with 50 to 75 percent stenosis and normal left ventricular function.

The outcomes of patients with LMCAD treated with CABG have improved over time. Reports of those who underwent CABG after 1995 suggest that the 30-day mortality ranges between 3 and 4.2 percent and the survival at two years is approximately 95 percent. Thirty-day mortality is now under 2 percent in some United States databases.

### PCI versus CABG :

CABG has a long track record of safety and efficacy in patients with LMCAD. The application of percutaneous coronary intervention (PCI) with stenting to the left main coronary artery began in patients who were not candidates for CABG. Randomized trials and observational studies have suggested equivalent outcomes with these two forms of revascularization in some patients with LMCAD.

We arrive at the following conclusions regarding the studies presented below comparing CABG with PCI with stenting. The odd ratios (OR) given below come from a 2016 meta-analysis of the four major randomized trials discussed below plus one smaller trial.

- At one year and longer, CABG and PCI appear to have similar rates of the combined end point of death from any cause, myocardial infarction (MI), and stroke (OR 0.97, 95% CI 0.79-1.17).
- As the complexity of associated

coronary artery disease increases, assessed either by the SYNTAX score or as the number of vessels that need revascularization, the benefit in favor of CABG over PCI with stenting increases.

For patients with lower complexity coronary disease who can undergo PCI at an acceptable risk and with reasonable probability for success, PCI may be an acceptable or even preferred option in some patients. Our experts prefer CABG for younger patients who have low surgical risk, for whom short-term surgical outcomes are favorable and potentially favorable long-term outcomes more meaningful.

- CABG is associated with a significantly higher incidence of adverse in-hospital outcomes, including death, MI, and stroke. However, the long-term rates of death, MI, and stroke are comparable or better depending on severity of associated coronary artery disease and possibly duration of follow-up.
- PCI with stenting is associated with a higher incidence of repeat (usually target vessel) revascularization at long-term follow-up (OR 1.85, 95% CI 1.53-2.23).

Randomized trials — The EXCEL, NOBLE, PRECOMBAT, and SYNTAX trials directly compared CABG with PCI with stenting. EXCEL and NOBLE are the most recent of these and were the only trials to use current generation drug eluting stents (DES) and thus these two trials have the greatest impact on our recommendations.

- The EXCEL trial randomly assigned 1905 patients with left main CAD of low or intermediate anatomical complexity (SYNTAX score of 32 or lower) to either PCI (with a goal of complete

revascularization) with everolimus-eluting stents or CABG.

The primary end point, a composite of death from any cause, stroke, or MI at three years, occurred at a similar rate in both groups (15.4 versus 14.7 percent; hazard ratio 1, 95% CI 0.79-1.26). There were no significant between-group differences in the three-year rates of the components of the primary end point. The secondary end point of death, stroke, or MI at 30 days occurred less often in patients in the PCI group (4.9 versus 7.9 percent) due mainly to a lower rate of MI. The secondary end point of death, stroke, MI, or ischemia driven revascularization at three years occurred more often with PCI (23.1 versus 19.1 percent)

- The NOBLE trial randomly assigned 1201 patients (without ST-elevation MI) to complete revascularization with either PCI, using a biolimus-eluting stent or CABG. The primary end point of major adverse cardiac or cerebrovascular events (a composite of all-cause mortality, nonprocedural MI, any repeat coronary revascularization, and stroke) at five years occurred more often with PCI (29 versus 19 percent; hazard ratio [HR] 1.48, 95% CI 1.11-1.96) attributable mainly to more frequent revascularization in the PCI group. There was also a higher rate of non-procedural MI and stroke, the latter of which is not consistent with all other trials.

- The PRECOMBAT trial randomly assigned 600 patients with unprotected LMCAD to PCI with sirolimus-eluting stents or CABG.

At two years, the event rates for the primary outcome were still higher but not significantly different with PCI (12.2 versus

8.1 percent with CABG). The difference between the two groups was due to a statistically significant higher rate of ischemia-driven target lesion revascularization with PCI (9 and 4.2 percent). The rates of stroke did not differ significantly (0.4 versus 0.7 percent).

At five years, the event rates for the primary outcome were 17.5 and 14.3 percent in the PCI and CABG groups, with the difference being not statistically different. Ischemia-driven target lesion revascularization remained the principal reason for the higher rate in the PCI group.

Consistent with other studies there was an advantage for CABG with left main plus three-vessel disease (HR 3.05, 95% CI 1.29-7.21).

- A subgroup analysis of the **SYNTAX** trial, which randomly assigned 1800 patients with multivessel or LMCAD to either stenting with a paclitaxel-eluting stent or CABG, evaluated outcomes in the 705 patients with LMCAD. Among patients with LMCAD, 35 percent had LMCAD alone or associated with single vessel disease.

In this subgroup analysis, the primary outcome, the 12-month rate of major adverse cardiac or cerebrovascular events (MACCE; death from any cause, stroke, MI, or repeat revascularization) was not significantly different in the PCI and CABG groups (15.8 versus 13.7 percent). Patients with PCI had a significantly higher rate of repeat revascularization (11.8 versus 6.5 percent).

**Outcomes according to the complexity of disease were evaluated and the following findings were noted:**

- The rate of the primary outcome with PCI increased significantly as the number of vessels with associated disease increased (7.1, 7.5, 19.8, and 19.3 percent for 0, 1, 2, and 3 vessel associated disease, respectively). The comparable rates for CABG patients were 8.5, 13.2, 14.4, and 15.4 percent, respectively.
- When grouped according to the SYNTAX score patients with low (<23) or intermediate (23 to 32) scores did not differ significantly with respect to the primary outcome comparing PCI with CABG. However, those with high (>32) scores had a significantly higher rate of the primary outcome with PCI (25.3 versus 12.9 percent).
- Five-year outcomes for the 705 patients in SYNTAX with LMCAD have been reported and are consistent with the findings at 12 months. The primary outcome (MACCE) was similar between the PCI and CABG groups (36.9 versus 31 percent, respectively; HR 1.23, 95% CI 0.95-1.59). In patients with low or intermediate SYNTAX scores, MACCE was similar between the two groups, but was significantly higher in PCI patients with scores  $\geq 33$  (46.5 versus 29.7 percent).

PCI with stenting — The application of PCI with stenting to the left main coronary artery began in patients who were not candidates for CABG. With improvement in outcomes, PCI has become a viable option for many patients with left main disease.

If left main PCI is being considered, it should not be performed immediately after coronary arteriography. The patient should hear opinions from a multidisciplinary team prior to deciding on a

revascularization strategy. Exceptions to this principle include patients who are unstable and need immediate revascularization in the catheterization laboratory or those in whom CABG is not an option for any reason.

The rate of target vessel revascularization is significantly lower with DES compared with bare metal (BMS) stents in patients with LMCAD. In almost all cases, we use DES and we prefer second generation DES.

**Non-distal lesions :** Data are limited regarding outcomes with PCI in patients who do not require stenting of the distal left main coronary artery, in part because this site is involved in the majority of cases. One observational study reported the following outcomes after placement of a DES in 146 patients who had left main lesions involving the ostium and/or the mid-shaft (non-bifurcation):

- In hospital, there were no cardiac deaths (one noncardiac death), no Q-wave MIs, and five non-Q-wave MIs (3.4 percent).
- In the 106 patients who underwent angiographic follow-up at four to six months, mean late lumen loss was 0.01 mm, and restenosis occurred in only one patient (0.9 percent).
- At a mean follow-up of 886 days, there were five deaths (3.4 percent cumulative mortality), one target lesion revascularization, and seven (4.7 percent) target vessel revascularizations.

**Distal lesions :**

The distal left main coronary artery is involved in the majority of cases (60 to 94 percent of lesions) and the results of PCI are worse than for lesions located at the ostium or mid-shaft. For patients with unprotected

distal left main disease and involvement of the origins of both the left anterior descending coronary artery and circumflex, we prefer a dedicated two-stent approach in most patients in whom PCI will be performed. Based on the results of the DKCRUSH-V trial discussed below, we believe the double kissing crush technique may be the best strategy. In cases where both origins are large and free of significant disease, a planned single stent strategy may still be the best option.

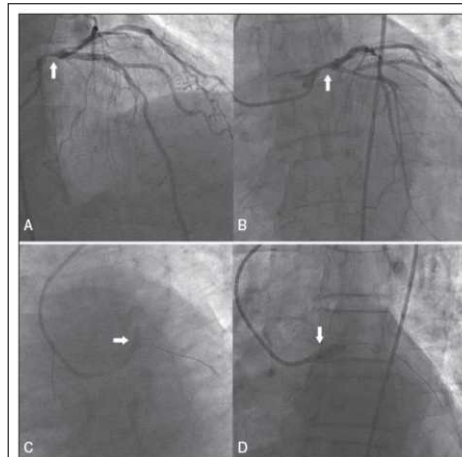
The overall rate of restenosis is low after stenting for LMCAD with rates of target lesion revascularization <5 percent for disease limited to the ostium or mid lesions and single stent approaches into the left anterior descending coronary artery. The rate of repeat target lesion revascularization is higher for distal lesions involving both origins with the circumflex origin especially vulnerable to recurrence. Outcomes in patients treated for distal disease have been evaluated in several older observational studies using first generation DES. In a retrospective cohort analysis that compared outcomes with one- or two-stent techniques for distal disease, the rate of all-cause death was around 15 percent, and the rate of target lesion revascularization was between 17 and 26 percent at five years.

The optimal stenting technique for distal left main lesions is not known. In many cases, the best approach may be determined by the specific anatomy. PCI of the distal left main coronary artery is technically challenging, and patients with potentially complicated anatomy should be treated only by highly skilled interventional cardiologists. The challenges are greater for bifurcation lesions involving both origins.

A variety of approaches to PCI of the distal left main coronary artery have been evaluated in clinical trials and these include:

- Provisional stenting (PS)
- The double kissing (DK)
- With the T stent technique,
- With the culotte technique,

Early studies suggested that outcomes were poorer when distal left main bifurcation lesions are treated by a two-stent approach (ie, crush or kissing stents) rather than with provisional stenting. In



**Figure 1) A and B Coronary angiography showing stenosis of the mid part of the left main coronary artery. C Stent deployment in the left main coronary artery. D Postdilation with a non compliant balloon.**

these early studies, the rate of target lesion revascularization (mostly by repeat catheter-based intervention with drug-eluting stents) was as high as 25 percent. Restenosis was essentially confined to distal lesions, the majority of which had been treated with stents in both branches. The following randomized trials have compared two of the approaches described above in patients with unprotected distal

left main bifurcation lesions:

- The **DKCRUSH-III** study randomly assigned 419 patients to a double kissing crush or a culotte technique. The primary composite end point (cardiac death, MI, and TVR at one year) occurred more often in the culotte group (16.3 versus 6.2 percent;  $p = 0.001$ ), attributable mainly to an increased rate of TVR (11 versus 4.3 percent). This trial does not address if either dedicated two-stent approach is superior to provisional stenting. This question was addressed in the DKCRUSH V trial.
- The **DKCRUSH-V** trial randomly assigned 482 patients to DK crush stenting or PS. At one year, the primary composite end point of target lesion failure (cardiac death, target vessel MI, or clinically driven target lesion revascularization) occurred less often with the latter (5.0 versus 10.7 percent; hazard ratio 0.42, 95% CI 0.21-0.85). The risk of target lesion revascularization was lower with the DK crush technique (3.8 versus 7.9 percent), as was the rate of (protocol-mandated) angiographic restenosis at 13 months (7.1 versus 14.6 percent).

#### Long-term outcomes :

The best available data for long-term outcomes with stenting of LMCAD come from the large EXCEL and NOBLE randomized trials, which compared PCI and CABG, discussed above.

#### Patients with acute MI :

There are limited data on the use of PCI in patients with acute MI due to LMCAD. Older small series noted in-hospital mortality rates of 30 to 35 percent following PCI with or without stenting. Not surprisingly, the outcomes in such patients

are worse than in those with LMCAD who undergo elective PCI. The cases reported represent a selected group that survived to reach the cardiac catheterization laboratory. More observational studies (2011) have reported lower in-hospital mortality rates, ranging from 11 to 21 percent.

More data are available in patients with cardiogenic shock complicating acute MI. In the SHOCK trial registry, 16 percent of patients had significant LMCAD (although not necessarily left main occlusion). Although the patients who underwent angiography had a lower baseline risk and better hemodynamic profile than those who did not, mortality in these patients was higher than in those with circumflex, left anterior descending coronary artery, or right coronary artery lesions (79 versus 37 to 42 percent).

The potential efficacy of PCI was illustrated in a report from an observational registry of patients with unprotected left main stenosis; 40 patients with an acute MI (37 of whom had cardiogenic shock) underwent emergency PCI (17 with stenting). The rates of in-hospital death (35 versus 70 percent) and need for CABG (6 versus 22 percent) were lower in those who received a stent compared with primary percutaneous transluminal coronary angioplasty alone. Stenting was also associated with a higher survival rate at 12 months (53 versus 35 percent).

The outcome of such protected left main interventions is more favorable than when there is no patent graft to the left coronary system (ie, unprotected). In essence, stenting in this circumstance is being performed for a single vascular territory

**LEFT MAIN EQUIVALENT DISEASE :** Left main equivalent disease, defined as severe ( $\geq 70$  percent) proximal left

anterior descending coronary artery and proximal left circumflex disease, carries a poor prognosis, although somewhat better than left main coronary artery disease. The largest experience with such patients comes from the CASS registry of 912 patients with left main equivalent disease. At more than 16-year follow-up, coronary artery bypass graft surgery (CABG) was associated with significant increases in mean survival (13.1 versus 6.2 years) and the likelihood of survival (44 versus 31 percent); 26 percent of medically treated patients ultimately underwent CABG.

## SUMMARY AND RECOMMENDATIONS

For patients with left main coronary artery disease (LMCAD), we recommend revascularization, as opposed to medical therapy (Grade 1A).

The composite outcome of death, myocardial infarction, and stroke is similar in patients with LMCAD who are treated with coronary artery bypass graft surgery (CABG) or percutaneous coronary intervention (PCI). However, the rate of target vessel revascularization is higher with PCI.

Some subgroups of patients with LMCAD are likely to do better with CABG

Those with associated two- or three-vessel disease, particularly those with either high risk scores, such as SYNTAX, or those who are unlikely to be fully revascularized with PCI.

Patients with poor left ventricular systolic function, such as those with a left ventricular ejection fraction of less than 30 percent, although these patients were not evaluated in the above randomized trials.

For patients with unprotected LMCAD who are reasonable surgical candidates:

CABG, as opposed to PCI, if there is

associated three-vessel disease or two-vessel disease with a high SYNTAX score (Grade 1B).

CABG as opposed to PCI in patients with left main only or one or two-vessel disease and a low SYNTAX score (Grade 2B). Those patients who have been fully informed of the relative benefits and risk of the two procedures and who have a strong preference to not undergo CABG may reasonably choose PCI.

In most cases, a thorough discussion of the relative risks and benefits of the two forms of revascularization should take place after coronary angiography between the patient and a healthcare team that involves an interventional cardiologist and a cardiothoracic surgeon at a minimum.

Some patients may proceed directly to PCI after coronary arteriography:

Patients presenting with acute coronary syndrome who have left main occlusion and who are hemodynamically unstable. Such patients require emergent revascularization, with PCI generally being the most expedient and safe choice.

Patients who are not surgical candidates who have been informed of the benefits and risks of PCI before the procedure.

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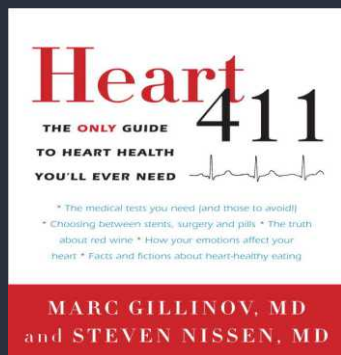
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