Evidence-Based Management of CAD: Last Decade Trials and Updated Guidelines

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Conflict of Interests

• No conflict of interests
2013 ESC guidelines on the management of stable coronary artery disease

The Task Force on the management of stable coronary artery disease of the European Society of Cardiology

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• Patients with stable angina or dyspnea;
• Patients previously symptomatic with known obstructive or non-obstructive CAD;
• Patients reporting symptoms for the first time.
DEFINITION

Disease that cause exercise- and stress-related chest pain due to narrowing of:

- ≥ 50% in left main coronary artery;
- ≥ 70% in one or several of the major coronary arteries.

What’s new? 2013

1. Not only narrowing but also microvascular dysfunction;
2. Increased importance to the pre-test probability of disease;
3. Increasing evidence that benefit of revascularization may be less than expected
SYMPTOMS

A careful medical history and a clear description of chest pain is mandatory to confirm diagnosis.

**Table 4: Traditional clinical classification of chest pain**

<table>
<thead>
<tr>
<th>Typical angina (definite)</th>
<th>Meets all three of the following characteristics:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• substernal chest discomfort of characteristic quality and duration;</td>
</tr>
<tr>
<td></td>
<td>• provoked by exertion or emotional stress;</td>
</tr>
<tr>
<td></td>
<td>• relieved by rest and/or nitrates within minutes.</td>
</tr>
</tbody>
</table>

| Atypical angina (probable) | Meets two of these characteristics. |

| Non-anginal chest pain | Lacks or meets only one or none of the characteristics. |

**Table 5: Classification of angina severity according to the Canadian Cardiovascular Society**

<table>
<thead>
<tr>
<th>Class I</th>
<th>Ordinary activity does not cause angina such as walking and climbing stairs. Angina with strenuous or rapid or prolonged exertion at work or recreation.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class II</td>
<td>Slight limitation of ordinary activity. Angina on walking or climbing stairs rapidly, walking or stair climbing after meals, or in cold, wind or under emotional stress, or only during the first few hours after awakening. Walking more than two blocks on the level and climbing more than one flight of ordinary stairs at a normal pace and in normal conditions.</td>
</tr>
<tr>
<td>Class III</td>
<td>Marked limitation of ordinary physical activity. Angina on walking one to two blocks on the level or one flight of stairs in normal conditions and at a normal pace.</td>
</tr>
<tr>
<td>Class IV</td>
<td>Inability to carry on any physical activity without discomfort – angina syndrome may be present at rest.</td>
</tr>
</tbody>
</table>

*Equivalent to 100–200 m.
DIAGNOSIS and ASSESSMENT

BASELINE TESTING

• Biochemical tests: hemoglobin, glycaemia, lipid profile, renal function, markers of myocardial injury.

• Resting ECG: 12-lead ECG, investigation of ST-changes, arrhythmias, branch blocks.

• Echocardiography.

• Cardiac MRI: structural abnormalities, LV function.

• (Chest X-Ray)
DIAGNOSIS and ASSESSMENT

STRESS TESTING

• ECG exercise testing: *simple and available, evaluation of exercise and recovery.*

• Stress Echocardiography: *exercise or pharmacological agents (dobutamine).*

• Myocardial Perfusion Scintigraphy: *evaluation of blood flow with regional tracer (99mTc) uptake.*

• Stress Cardiac Magnetic Resonance: *wall motion abnormalities with dobutamine infusion.*

• Hybrid techniques: SPECT/CT, PET/CT, PET/CMR (in selected centers)
CORONARY ANATOMY

DIAGNOSIS and ASSESSMENT

NON-INVASIVE TECHNIQUES:

- Coronary CT-scan: 64-slice CT
- Calcium Score: detection of coronary calcification without contrast
- Coronary MRI angiography

INVASIVE TECHNIQUES:

- Coronary Angiography: coronary anatomy, flow, FFR
DIAGNOSIS and ASSESSMENT

MAJOR STEPS FOR DECISION-MAKING:

**STEP 1**: clinical assessment of the probability that CAD is present.

**STEP 2**: non-invasive testing to establish the diagnosis.

**STEP 3**: optimal therapy and stratification for risk of subsequent events.
Figure 1: Initial diagnostic management of patients with suspected SCAD. CAD = coronary artery disease; CTA = computed tomography angiography; CXR = chest X-ray; ECG = electrocardiogram; ICA = invasive coronary angiography; LVEF = left ventricular ejection fraction; PTP = pre-test probability; SCAD = stable coronary artery disease.

a May be omitted in very young and healthy patients with a high suspicion of an extracardiac cause of chest pain and in multimorbid patients in whom the echo result has no consequence for further patient management.

b If diagnosis of SCAD is doubtful, establishing a diagnosis using pharmacologic stress imaging prior to treatment may be reasonable.
STRATIFICATION for RISK of EVENTS

Avoiding risk of CV-death and MI:

• Risk stratification by clinical evaluation
• Risk stratification by ventricular function
• Risk stratification by response to stress testing
• Risk stratification by coronary anatomy
Confirmed diagnosis SCAD

- PTP 15–85% → test information will already be available
- PTP >85% → additional testing for risk stratification only in patients who have mild symptoms with medical management but following adequate information wish to proceed to revascularization in case of high risk

Low event risk (mortality <1%/year)

Intermediate event risk (mortality ≥1% but <3%/year)

High event risk (mortality ≥3%/year)

OMT and consider ICA (based on co-morbidities and patient preferences)

ICA (+ FFR when required) (+ revascularization when appropriate) + OMT

Trial of OMT

Continue OMT

Symptoms improved?

Yes

No

Intensify medical treatment

Symptoms improved?

Yes

No

Figure 3  Management based on risk determination for prognosis in patients with chest pain and suspected SCAD (for choice of test see Fig. 2, for definitions of event risk see Table 17). ICA = invasive coronary angiography; OMT = optimal medical therapy; PTP = pre-test probability; SCAD = stable coronary artery disease.
LIFESTYLE MANAGEMENT

- **Smoking**: quitting smoking is potentially the most effective of all preventive measures.

- **Diet**: weight (BMI < 25) and lipid (**LDL < 70 mg/dL**) management.

- **Physical activity**: associated with less CV mortality and morbidity.

- **Arterial Hypertension**: systolic BP < 140 mmHg, diastolic BP < 90 mmHg.

- **Diabetes**

- **Psychosocial factors**: depression anxiety and distress.
1. **Anti-platelet agents**: low-dose aspirin, clopidogrel, thienopyridine.

2. **Heart rate control**: B-blockers, calcium channel blockers

3. **Blood pressure control**: ACEi, ARB.

**EVENT PREVENTION**
REVASCULARIZATION

**Percutaneous Coronary Intervention (PCI)**
choosing the best stent (BMS vs DES)
antiplatelet therapy.

**Bypass Surgery**
arterial vs vein grafts, single vs bilateral IMA, on-pump vs off-pump
**Figure 5** Global strategy of intervention in stable coronary artery disease (SCAD) patients with demonstrated ischaemia. CABG = coronary artery bypass graft; CAD = coronary artery disease; LAD = left anterior descending; LV = left ventricular; OMT = optimal medical treatment; PCI = percutaneous coronary intervention.

*Indication of revascularization for prognosis or symptoms (see Table 32).

*Not suitable for revascularization due to anatomy or clinical conditions.

See section 9.
Revascularization vs Medical Therapy

• In low-risk patients, the strategy of initial medical therapy is safe and should be the default approach.

• When MT has failed and patients remain symptomatic, the various options need to be discussed by the Heart Team.
PCI vs BYPASS SURGERY

1. Importance of the hospital Heart Team.

2. Importance of optimal medical therapy in all patients for both groups.

3. **SINTAX Study**: in selected patients (score >33) higher incidence of stroke with CABG, repeating revascularization lower with CABG, higher survival rate with CABG.

4. **Hybrid Revascularization**: allows complete revascularization with the advantages of both techniques.
PCI vs BY-PASS SURGERY

Figure 6 Percutaneous coronary intervention (PCI) or coronary artery bypass graft surgery (CABG) in stable coronary artery disease without left main coronary artery involvement. CABG = coronary artery bypass graft; LAD = left anterior descending; PCI = percutaneous coronary intervention.

*a > 50% stenosis and proof of ischaemia, > 90% stenosis in two angiographic views, or FFR = 0.80.
*b CABG is the preferred option in most patients unless patients co-morbidities or specificities deserve discussion by the heart team. According to local practice (time constraints, workload) direct transfer to CABG may be allowed in these low risk patients, when formal discussion in a multidisciplinary team is not required (adapted from ESC/EACTS Guidelines on Myocardial Revascularization 2010).
PCI vs BY-PASS SURGERY

Figure 7. Percutaneous coronary intervention (PCI) or coronary artery bypass graft surgery (CABG) in stable coronary artery disease with left main coronary artery involvement. CABG = coronary artery bypass graft; PCI = percutaneous coronary intervention.

*a* >50% stenosis and proof of ischaemia, >70% stenosis in two angiographic views, or fractional flow reserve = 0.80.

*b* Preferred option in general. According to local practice (time constraints, workload) direct decision may be taken without formal multidisciplinary discussion, but preferably with locally agreed protocols (adapted from ESC/EACTS Guidelines on Myocardial Revascularization 2010).
• Importance of the Heart Team in the decision making process.
## PCI vs BY-PASS SURGERY

Recommendation for the type of revascularization (CABG or PCI) in patients with SCAD with suitable coronary anatomy for both procedures and low predicted surgical mortality

<table>
<thead>
<tr>
<th>Recommendations according to extent of CAD</th>
<th>CABG</th>
<th>PCI</th>
</tr>
</thead>
<tbody>
<tr>
<td>One or two-vessel disease without proximal LAD stenosis.</td>
<td>IIb</td>
<td>C</td>
</tr>
<tr>
<td>One-vessel disease with proximal LAD stenosis.</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>Two-vessel disease with proximal LAD stenosis.</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Left main disease with a SYNTAX score ≤ 22.</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Left main disease with a SYNTAX score 23–32.</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Left main disease with a SYNTAX score &gt;32.</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Three-vessel disease with a SYNTAX score ≤ 22.</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>Three-vessel disease with a SYNTAX score 23–32.</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>Three-vessel disease with a SYNTAX score &gt;32.</td>
<td>I</td>
<td>A</td>
</tr>
</tbody>
</table>

CABG = coronary artery bypass grafting; LAD = left anterior descending coronary artery; PCI = percutaneous coronary intervention; SCAD = stable coronary artery disease.

*Class of recommendation.

Level of evidence.

References
### Procedural aspects of CABG

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>It is recommended to perform procedures in a hospital structure and by a team specialized in cardiac surgery, using written protocols.</td>
<td>I</td>
<td>B</td>
<td>635,636</td>
</tr>
<tr>
<td>Endoscopic vein harvesting should be considered to reduce the incidence of leg wound complications.</td>
<td>IIa</td>
<td>A</td>
<td>577,578,580–582, 637,638</td>
</tr>
<tr>
<td>Routine skeletonized IMA dissection should be considered.</td>
<td>IIa</td>
<td>B</td>
<td>586–589</td>
</tr>
<tr>
<td>Skeletonized IMA dissection is recommended in patients with diabetes or when bilateral IMAs are harvested.</td>
<td>I</td>
<td>B</td>
<td>586–589</td>
</tr>
<tr>
<td><strong>Complete myocardial revascularization is recommended.</strong></td>
<td>I</td>
<td>B</td>
<td>594,598,600</td>
</tr>
<tr>
<td><strong>Arterial grafting with IMA to the LAD system is recommended.</strong></td>
<td>I</td>
<td>B</td>
<td>602,603,639</td>
</tr>
<tr>
<td>Bilateral IMA grafting should be considered in patients &lt;70 years of age.</td>
<td>IIa</td>
<td>B</td>
<td>165,606–610,640, 641</td>
</tr>
<tr>
<td>Use of the radial artery is recommended only for target vessels with high-degree stenosis.</td>
<td>I</td>
<td>B</td>
<td>618,642</td>
</tr>
<tr>
<td>Total arterial revascularization is recommended in patients with poor vein quality independently of age.</td>
<td>I</td>
<td>C</td>
<td>-</td>
</tr>
<tr>
<td>Total arterial revascularization should be considered in patients with reasonable life expectancy.</td>
<td>IIa</td>
<td>B</td>
<td>643</td>
</tr>
<tr>
<td>Minimization of aortic manipulation is recommended.</td>
<td>I</td>
<td>B</td>
<td>442,644</td>
</tr>
<tr>
<td>Off-pump CABG should be considered for subgroups of high-risk patients in high-volume off-pump centres.</td>
<td>IIa</td>
<td>B</td>
<td>626,627,629</td>
</tr>
<tr>
<td>Off-pump CABG and/or no-touch on-pump techniques on the ascending aorta are recommended in patients with significant atherosclerotic disease of the ascending aorta in order to prevent perioperative stroke.</td>
<td>I</td>
<td>B</td>
<td>443</td>
</tr>
<tr>
<td>Minimally invasive CABG should be considered in patients with isolated LAD lesions.</td>
<td>IIa</td>
<td>C</td>
<td>643</td>
</tr>
<tr>
<td>Electrocardiogram-triggered CT scans or epicardial scanning of the ascending aorta should be considered in patients over 70 years of age and/or with signs of extensive generalized atherosclerosis.</td>
<td>IIa</td>
<td>C</td>
<td>-</td>
</tr>
<tr>
<td>Routine intraoperative graft flow measurement should be considered.</td>
<td>IIa</td>
<td>C</td>
<td>-</td>
</tr>
</tbody>
</table>

**CABG** = coronary artery bypass grafting; **CT** = computed tomography; **IMA** = internal mammary artery; **LAD** = left anterior descending.
CLINICAL TRIALS

- PCI (DES) vs CABG in LM disease.
- Meta-analysis including 4392 pts.
- 4 randomized trials
- Similar long-term outcomes (death, MI, stroke).
- CABG was associated with a significant reduction in the risk of repeated revascularization.
CLINICAL TRIALS

Long-term outcomes of coronary artery bypass grafting versus stent-PCI for unprotected left main disease: a meta-analysis

Salvatore De Rosa, Alberto Polimeni, Jolanda Sabatino and Ciro Indolfi

Abstract

Background: Coronary artery bypass graft (CABG) surgery has traditionally represented the standard of care for left main coronary artery (LMCA) disease. However, percutaneous coronary intervention with stent implantation (PCI) has more recently emerged as a valuable alternative. The long-time awaited results of the largest randomized trials on the long-term impact of PCI versus CABG in LMCA disease, the newly published NOBLE and EXCEL studies, revealed contrasting results. Thus, aim of the present meta-analysis was to review the most robust evidence from randomized comparisons of CABG versus PCI for revascularization of LMCA.

Methods: Randomized studies comparing long-term clinical outcomes of CABG or Stent-PCI for the treatment of LMCA disease were searched for in PubMed, the Chochrane Library and Scopus electronic databases. A total of 5 randomized studies were selected, including 4499 patients.

Results: No significant difference between CABG and PCI was found in the primary analysis on the composite endpoint of death, stroke and myocardial infarction (OR = 1.06 95% CI 0.80–1.40; p = 0.70). Similarly, no differences were observed between CABG and PCI for all-cause death (OR = 1.03 95% CI 0.81–1.32; p = 0.81). Although not statistically significant, a lower rate of stroke was registered in the PCI arm (OR = 0.86; p = 0.67), while a lower rate of myocardial infarction was found in the CABG arm (OR = 1.43; p = 0.17). On the contrary, a significantly higher rate of repeat revascularization was registered in the PCI arm (OR = 1.76 95% CI 1.45–2.13; p < 0.001).

Conclusions: The present meta-analysis, the most comprehensive and updated to date, including 5 randomized studies and 4499 patients, demonstrates no difference between Stent-PCI and CABG for the treatment of LMCA disease in the composite endpoint of death, stroke and myocardial infarction. Hence, a large part of patients with unprotected left main coronary artery disease can be managed equally well by means of both these revascularization strategies.

Keywords: LMCA, CABG, PCI

• PCI (DES) vs CABG in LM disease.
• Meta-analysis including 4499 pts.
• 5 randomized trials
• Lower rate of stroke in PCI arm (not SS)
• Lower rate of MI in the CABG arm (not SS)
• CABG was associated with a significant reduction in the risk of repeated revascularization.
CLINICAL TRIALS

Clinical outcomes with percutaneous coronary revascularization vs coronary artery bypass grafting surgery in patients with unprotected left main coronary artery disease: A meta-analysis of 6 randomized trials and 4,686 patients

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Background Some but not all randomized controlled trials (RCT) have suggested that percutaneous coronary intervention (PCI) with drug-eluting stents may be an acceptable alternative to coronary artery bypass grafting (CABG) surgery for the treatment of unprotected left main coronary artery disease (ULMCD). We therefore aimed to compare the risk of all-cause mortality between PCI and CABG in patients with ULMCD in a pairwise meta-analysis of RCT.

Methods Randomized controlled trials comparing PCI vs CABG for the treatment of ULMCD were searched through MEDLINE, EMBASE, Cochrane databases, and proceedings of international meetings.

Results Six trials including 4,686 randomized patients were identified. After a median follow-up of 39 months, there were no significant differences between PCI vs CABG in the risk of all-cause mortality (hazard ratio [HR] 0.99, 95% CI 0.76-1.30) or cardiac mortality. However, a significant interaction for cardiac mortality (Pinteraction = 0.03) was apparent between randomization arm and SYNTAX score, such that the relative risk for mortality tended to be lower with PCI compared with CABG among patients in the lower SYNTAX score tertile, similar in the intermediate tertile, and higher in the upper SYNTAX score tertile. Percutaneous coronary intervention compared with CABG was associated with a similar long-term composite rate of death, myocardial infarction, or stroke (HR 1.06, 95% CI 0.82-1.37), with fewer events in 30 days after PCI offset by fewer events after 30 days with CABG (Pinteraction = 0.001). Percutaneous coronary intervention was associated with greater rates of unplanned revascularization compared with CABG (HR 1.74, 95% CI 1.47-2.07).

Conclusions In patients undergoing revascularization for ULMCD, PCI was associated with similar rates of mortality compared with CABG at a median follow-up of 39 months, but with an interaction effect suggesting relatively lower mortality with PCI in patients with low SYNTAX score and relatively lower mortality with CABG in patients with high SYNTAX score. Both procedures resulted in similar long-term composite rates of death, myocardial infarction, or stroke, with PCI offering an early safety advantage and CABG demonstrating greater durability. (Am Heart J. 2017 Aug;190:54-63.)

• PCI (DES) vs CABG in LM disease.
• Meta-analysis including 4686 pts.
• 6 randomized trials.
• Similar long-term outcomes (death, MI, stroke).
• Relatively lower mortality with PCI in patients with low SINTAX score and relatively lower mortality with CABG in patients with higher SINTAX score.
• CABG demonstrates greater durability.

CLINICAL TRIALS

Comparison of Stenting Versus Bypass Surgery According to the Completeness of Revascularization in Severe Coronary Artery Disease

Patient-Level Pooled Analysis of the SYNTAX, PRECOMBAT, and BEST Trials

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ABSTRACT

OBJECTIVES The aim of this study was to compare long-term survival between patients with severe coronary artery disease undergoing coronary artery bypass grafting (CABG) and those undergoing percutaneous coronary intervention (PCI) achieving complete revascularization (CR) or incomplete revascularization.

BACKGROUND The importance of CR in decision making regarding revascularization strategy in patients with severe coronary artery disease is unknown.

METHODS Data were pooled from the SYNTAX (Synergy Between PCI With Taxus and Cardiac Surgery), PRECOMBAT (Premier of Randomized Comparison of Bypass Surgery Versus Angioplasty Using Sirolimus-Eluting Stent in Patients With Left Main Coronary Artery Disease), and BEST (Randomized Comparison of Coronary Artery Bypass Surgery and Everolimus-Eluting Stent Implantation in the Treatment of Patients With Multivessel Coronary Artery Disease) trials. The primary outcome was death from any cause and was compared in an as-treated analysis.

RESULTS The rate of CR was 81.7% (79.2% with PCI and 66.2% with CABG). During a median 4.9-year follow-up period (interquartile range: 4.5 to 5.0 years), compared with patients undergoing CABG with CR, those undergoing PCI with incomplete revascularization had a higher risk for death from any cause (adjusted hazard ratio [aHR]: 1.43; 95% confidence interval [CI]: 1.03 to 2.00; p = 0.036) and the composite of death, myocardial infarction, and stroke (aHR: 1.48; 95% CI: 1.14 to 1.92; p = 0.003). However, there was no significant difference between patients undergoing CABG with CR and those undergoing PCI with CR regarding the risk for death from any cause (aHR: 1.16; 95% CI: 0.83 to 1.62; p = 0.39) and the composite of death, myocardial infarction, and stroke (aHR: 1.14; 95% CI: 0.87 to 1.48; p = 0.35). Subgroup analysis of multivessel coronary disease, high SYNTAX score (>32), and diabetes showed consistent findings.

CONCLUSIONS For the treatment of left main or multivessel coronary artery disease, PCI resulting in CR was associated with a similar long-term survival to CABG resulting in CR. Therefore, the ability to achieve CR should enter into the decision algorithm for choice of revascularization strategy. (J Am Coll Cardiol Intv. 2017;10:1415-24) © 2017 Published by Elsevier on behalf of the American College of Cardiology Foundation.

- PCI vs CABG for complete myocardial revascularization (CR).
- SYNTAX, PRECOMBAT, BEST trials.
- CR in PCI: 57%; CR in CABG: 67%.
- CR in CABG vs IR in PCI showed higher risk for death, MI and stroke in the PCI group.
- CR in CABG vs CR in PCI showed similar long-term survival rate.
Conclusion

• CABG in LM is associated with low risk of repeated revascularization but in some cases PCI is also an option
• In case of complete revasc. PCI and CABG showed same results in trials. CR is achieved more often with CABG.
• If completed revasc. is not achieved, CABG is superior to PCI
• CABG is clearly indicated in:
  • 3-V coronary disease (Syntax>23)
  • 1 or 2-V disease with proximal LAD (Heart Team)
  • LM disease + 2 or 3-V disease (Syntax>33 or Heart Team)
Heart Team: Joint Position of the Swiss Society of Cardiology and the Swiss Society of Cardiac Surgery.

Pedrazzini GB¹, Ferrari E², Zellweger M¹, Genoni M².

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Thank You