Review Article

Stable Coronary Artery Disease: Latest Data in the Battle Between Conservative and Invasive Management

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Myocardial revascularisation has been an established mainstay therapy for coronary artery disease (CAD) since the late 1960s. Rene Favoloro introduced CABG into clinical practice in 1967[1] and since then it has been the most intensively studied surgical procedure. Percutaneous revascularisation techniques have been in use for 35 years and have been subjected to more randomised studies (RCTs) than any other interventional procedure. Balloon angioplasty (PTCA) was used for the first time in 1977, by Andreas Gruentzig of Germany, as a non-surgical method for coronary artery revascularisation and in the mid 1980s it was proposed as an alternative therapy to coronary artery bypass grafting (CABG). Both reperfusion methods entail procedural risks that differ with respect to their nature, incidence, and time distribution.

While both procedures have seen significant technological advances, their role in the management of patients with stable CAD has been called into question by progress in medical treatment, also known as optimal medical therapy (OMT), which includes radical modification of cardiovascular risk factors and lifestyle in combination with intensive pharmacological management. These important developments in all three therapeutic strategies have relegated the findings of older studies to being of solely historical interest.

Evidence-based findings for myocardial revascularisation

Evidence-based findings for myocardial revascularisation come from RCTs and large, propensity-matched observational registries; both have advantages, but also limitations.

RCTs and their meta-analyses represent the highest hierarchical form of evidence-based medicine.[2,3] However, extrapolating their findings to daily clinical practice is complicated by the fact that their patient populations are not generally representative of the population encountered in real life. For example, most RCTs of PCI and CABG in multi-vessel CAD included less than 10% of potentially eligible patients, most of whom had 1- or 2-vessel disease. In addition, an 'intent to treat' analysis becomes problematic when many patients cross from the medication arm to the revascularisation arm. Moreover, the limited follow-up time (usually less than 5 years) tends to inflate the benefits of CABG, which, though superior initially, with the passage of time and progressive damage to venous grafts may not be so advantageous compared to PCI.

In contrast, taking data from all interventions, the large registries reflect daily clinical practice with greater accuracy. However, in the absence of randomisation, their main limitation is that they cannot take into account all the confounding factors that might affect both the choice and the outcome of different therapeutic interventions. Propensity matching, for both cardiac and extracardiac comorbidity, can only partly moderate this problem. Accepting this limitation, the independent registries have all reported that an initial strategy of CABG rather than PCI, in propensity matched patients with multi-vessel or main stem CAD, improves survival by 5% over a period of 3 to 5 years and is associated with a three- to six-fold reduction in the need for re-intervention.[4-9] The different populations in RCTs and registries could partly explain the apparent differences in effectiveness between the two procedures that we find in the literature.

OMT versus PCI

The effectiveness of PCI (with or without stenting) versus OMT has been evaluated in many meta-analyses[10-15] and in the large, randomised COURAGE trial.[16]

Most of the meta-analyses reported no difference in total and cardiovascular mortality, a greater incidence of non-fatal peri-procedural myocardial infarction, a reduced need for repeat revascularisation, and no difference in angina relief in the PCI arm. Only the meta-analysis of Schömig et al,[12] which included 17 RCTs, showed a survival benefit for PCI compared with OMT alone (respective mortalities 7.4% versus 8.7% over 51 months' follow up), but this study included in the revascularisation group patients with a recent myocardial infarction, as well as patients who underwent CABG. However, a meta-analysis by Jeremias et al[3] of 28 trials including a total of 13,121 patients reported lower mortality in the PCI group compared to OMT alone, over a mean follow-up period of 3 years (hazard ratio, HR 0.82, 95% confidence interval, CI: 0.68-0.99).

The COURAGE trial[16] randomised 2287 patients with known stable CAD and objective findings of myocardial ischaemia to OMT alone, or in combination with PCI. Over a 4.6-year follow up, there was no significant difference in the primary composite endpoint of death, myocardial infarction, stroke, or rehospitalisation for unstable angina. At one year, freedom from angina was greater by 12% in the PCI group; however, at 5 years this benefit had disappeared, while 21% of the PCI group and 33% of the OMT group underwent repeat revascularisation ($p<0.001$). Thus, this study showed that, in patients with chronic stable CAD, OMT is comparable to PCI as regards the risk of death, myocardial infarction or major adverse cardiovascular events (MACE).

However, in the COURAGE trial[16] the severity of the coronary artery disease was rather moderate—the incidences of 1-, 2- and 3-vessel disease being 31%, 39% and 30%, respectively—while only 31% of the patients had disease of the proximal part of the anterior descending artery. Furthermore, patients with main stem disease were excluded and most patients had normal left ventricular function, while 40% of the patients in the medication arm underwent revascularisation procedures during the follow-up period because of symptoms that were not controlled by drug treatment alone.

Altogether, the above data have led guideline groups to recommend OMT for the initial management of stable angina, with revascularisation reserved principally for patients whose symptoms are not satisfactorily controlled.

Balloon angioplasty versus bare-metal stents versus drug-eluting stents

Brophy et al,[17] in a meta-analysis of 29 studies that included a total of 9918 patients, found no difference between bare-metal stents (BMS) and PTCA as regards death, myocardial infarction, or need for CABG, although there was an absolute reduction of 5% in restenosis rate in the stented group.

Subsequent meta-analyses[18] of RCTs that compared drug-eluting stents (DES) with BMS reported no differences in the rates of death, cardiac death, or non-fatal myocardial infarction, although there was a significantly reduced need for target vessel revascularisation with the use of DES. In contrast, Kirtane et al,[19] in an unadjusted analysis of 182,901 patients in 34 observational studies of BMS and DES, reported significantly lower rates of mortality (HR 0.78, 95% CI: 0.71-0.86) and myocardial infarction (HR 0.87, 95% CI: 0.78-0.97) associated with DES implantation. However, after multivariable adjustment, the benefits of DES decreased significantly, and the possibility cannot be ruled out that their benefit was partly due to the simultaneous prolonged dual antiplatelet therapy.

The above findings are reflected in the recent network meta-analysis by Trikalinos et al[13] that in-

cluded 61 studies, involving a total of 25,388 patients with chronic CAD, from the earliest use of balloon angioplasty to the present era of BMS and DES. The researchers found no difference in terms of risk of death or myocardial infarction between drug therapy, PTCA, and PCI with BMS or DES, although there was a progressive and significant reduction in the need for repeat revascularisation: BMS vs. PTCA relative risk (RR) 0.68, 95%CI: 0.60-0.77; DES vs. BMS RR 0.44, 95% CI 0.35-0.56; DES vs. PTCA RR 0.30, 95% CI 0.17-0.51.

CABG versus drug therapy

The superiority of CABG over medical therapy in treating certain subgroups of patients with stable CAD was confirmed persuasively by Jusuf et al[20] in a meta-analysis of seven RCTs that is still the main legacy for modern CABG. The study revealed a survival benefit for CABG in patients with main stem or 3-vessel CAD, especially when the proximal segment of the anterior descending artery was involved. The benefits were greater in patients with severe symptoms, with early positive stress tests, and with impaired left ventricular performance, as well as in diabetic patients, as shown by the BARI trial.[21] The relevance of these findings to modern practice is being increasingly questioned, since the medications used in those studies were significantly inferior to modern OMT. Indeed, in the recently published STICH trial[22] 1212 patients with multi-vessel disease and severely impaired left ventricular function (ejection fraction <35%) were randomised to CABG or OMT to test whether surgical revascularisation would improve survival. After nearly 5 years' follow up, all-cause mortality (the primary endpoint) was similar between the groups, both in the main trial cohort and in a subgroup with demonstrable myocardial viability. As the editorialist commented, contemporary OMT should not be underestimated in the management of severe CAD.[23]

However, the recent meta-analysis by Jeremias et al[3] reported a lower risk of death for CABG compared to OMT (HR 0.63, 95% CI: 0.50-0.77). Moreover, these findings were confirmed in the recent BARI-2D trial,[24] which included 2368 diabetic type 2 patients (31% with 3-vessel disease). Patients were stratified as being eligible for either PCI or CABG and were then randomised to contemporary OMT or revascularisation. After an average of 5.3 years' follow up, rates of all-cause mortality (the primary end point) were similar for the medical and revascularisation groups, but in the CABG stratum, patients assigned to revascularisation had lower cardiovascular event rates (death, myocardial infarction or stroke) than patients assigned to OMT.

PCI versus CABG

Isolated disease of the proximal anterior descending artery

Aziz et al[25] and Kapoor et al[26] reported two meta-analyses of more than 3000 patients over a 5-year follow up, both of which reported no significant differences in safety endpoints (mortality, myocardial infarction, stroke) between PCI and CABG. However, they observed a threefold higher rate of recurrence of angina and a fivefold higher rate of target vessel revascularisation in the PCI patients. Similar findings were reported from a smaller study of 711 patients, who were treated with minimally invasive direct aortocoronary bypass or with stenting (predominantly BMS) and were followed for more than 2 years. The rates of death and myocardial infarction were similar in the two groups, apart from revascularisations, which were significantly fewer in the surgical group.[27]

Multi-vessel coronary artery disease

There are more than 15 studies of PCI versus CABG in multi-vessel CAD,[28] and only one study of OMT versus CABG (MASS II).[29] Most of the patients in these RCTs had essentially normal left ventricular systolic performance, with 1- or 2-vessel CAD and without involvement of the anterior descending artery.

The meta-analysis of these RCTs carried out by Hlatky et al[2] reported that CABG resulted in a fivefold reduction in the need for re-intervention, with no or moderate benefit in terms of survival, or a survival benefit only in patients aged >65 years (HR 0.82) and in diabetic patients (HR 0.7).

Hueb et al[30] recently reported the results from a 10-year follow up of patients in the MASS II randomised trial. The unique feature of that study was the fact that it included an arm with exclusively drug therapy for the treatment of patients with multi-vessel CAD. Thus, in one centre 611 patients were randomised to either CABG (203 patients), PCI with BMS (205 patients) or OMT alone (203 patients). These were patients with anatomically severe CAD, given that 93% had involvement of the proximal an-

terior descending artery, 58% had 3-vessel disease and 42% 2-vessel disease. All the patients had a normal ejection fraction and about 30% were diabetics. The primary endpoint of the study (a composite of total deaths, Q-wave myocardial infarction, or refractory angina requiring revascularisation) occurred more often in the drug group than in the CABG group (RR 2.35, 95% CI: 1.78-3.11) and more often in the PCI group than in the CABG group (RR 1.85, 95% CI: 1.39-2.47). In addition, the 10-year angina-free rates were 64% for CABG, 59% for PCI, and 43% for drug therapy ($p<0.001$). The researchers determined that, compared to CABG, drug therapy was associated with a higher incidence of myocardial infarction, higher rates of repeat revascularisation, a higher rate of cardiac death, and a 2.29 times greater risk of combined events. PCI was associated with a greater need for repeat revascularisation, a higher incidence of myocardial infarction, and a 1.46 times greater risk of combined events compared to CABG. In addition, CABG proved to be superior to drug therapy in eliminating anginal symptoms. No statistically significant difference was found as regards total mortality among the three therapeutic strategies, although the study was not designed to show differences in mortality. The superiority of revascularisation compared with drug therapy in the MASS II trial is in conflict with the findings of the COURAGE trial referred to above. Of course, the difference could probably be explained by the different patient populations in the two studies. Indeed, the anatomical complexity of the CAD was much greater in the MASS II trial and came close to the anatomical characteristics of the patients in the SYNTAX trial, which will be analysed below. In the COURAGE trial, one third of the patients had 1-vessel disease, while in the MASS II trial no patient had 1-vessel disease. Furthermore, only one third of the COURAGE patients had involvement of the proximal anterior descending artery, as against 92% in the MASS II trial.

The SYNTAX study

In contrast to the previous RCTs with highly selected patient groups, the SYNTAX study is a 5-year follow up of "all patients" with the most severe CAD, including patients with main stem disease and/or 3-vessel disease, who were enrolled either in a randomised arm, or in a parallel registry if they were not eligible for randomisation. Thus, the SYNTAX trial, having two components, recorded the real therapeutic decisions in a study of 1800 patients who were randomised to PCI or CABG and a registry of 1077 CABG patients (the complexity of whose CAD rendered them ineligible for PCI) and 198 PCI patients (who were considered to be at unacceptably high risk for surgery).

At one year,[31] 12.4% of the CABG and 17.8% of the PCI patients reached the respective primary composite endpoint of MACE ($p<0.002$), which included death (3.5% vs. 4.4%, $p=0.37$), myocardial infarction (3.3% vs. 4.8%, $p=0.11$), stroke (2.2% vs. 0.6%, $p=0.003$) and repeat revascularisation (5.9% vs. 13.5%, $p<0.001$).

The results at 3 years, which were announced at the European Congress of Cardiology in 2010 in Stockholm and were published recently in the European Heart Journal,[32] were similar to those from the first and second years of follow up. The total incidence of MACE remained significantly higher in the PCI arm compared to CABG, mainly because of the greater number of repeat revascularisations. In addition, the rates of MACE at 3 years were not significantly different in patients who had an initial low SYNTAX score (0-22). However, in the patients who had an intermediate (23-32) or high (≥33) SYNTAX score the MACE were significantly more frequent in the PCI group, although the safety endpoint (death, myocardial infarction or stroke) was still similar in the CABG and PCI groups (12% vs. 14.12%, $p=0.21$). In the PCI arm there was a significantly greater incidence of myocardial infarction compared with CABG, a finding that was not present in the first year of follow up and was due to an increase in the number of infarctions and repeat PCI procedures from the first to the third year. The incidence of stroke no longer differed between the two groups; the difference was only significant during the first year, because of the large number of strokes that occurred during the CABG procedure.

The results from an analysis of the registries showed that the total incidence of MACE at 12 months was 20.4% in the PCI registry and 8.8% in the CABG registry, findings similar to those in the randomised trial. The same picture continued over 3 years' follow up, during which the incidence of MACE almost doubled in both groups: 16.4% for CABG and 38% for the PCI registry.

Of course, we should stress that this study did not manage to achieve its primary goal, namely to demonstrate the non-inferiority of PCI over a 1-year fol-

low up. The high revascularisation rates in the PCI group were the reason for the negative results. Although the difference in MACE at 1 year between CABG and PCI was of the order of 5.5%, the 95% CI reached 8.3%, thus greatly exceeding the predetermined limit for non-inferiority of PCI, which was 6.6%. Since PCI failed to satisfy the predefined non-inferiority criteria, the researchers concluded that, at 1, 2 and 3 years, "CABG remains the main treatment for the management of patients with main stem disease or 3-vessel disease, especially in complex lesions (intermediate and high scores), although the difference in the primary endpoint of the study was largely due to the higher number of repeat revascularisations in the PCI arm." However, the fact that the safety endpoint did not differ between the 2 groups means that PCI is an acceptable alternative to CABG as a revascularisation method in patients with less complex disease (low SYNTAX scores).

The inability of the study to attain the non-inferiority criterion means that all the other findings are simple observations, susceptible to chance. Nonetheless, in the 1095 patients with 3-vessel coronary artery disease, the rates of MACE were 14.4% versus 23.8% in favour of CABG ($p<0.001$). Only in the third of patients with the lowest SYNTAX score (<23) was there no significant difference in MACE between the 2 groups. It is also noteworthy that the rates of death and repeat revascularisation were similar in the 1077 patients in the CABG registry, even though these patients had more complex coronary artery disease.

Totalling the 1665 patients with 3-vessel disease (1095 in the randomised trial and 570 in the registry), it appears that CABG offers a significantly better outcome at 1 and 2 years in patients with a SYNTAX score >22 (79% of the patients with 3-vessel disease). These results are compatible with those from previous studies, which report a survival benefit and a significant reduction in the need for repeat revascularisation for CABG compared to PCI in patients with more severe coronary artery disease.

More recently, an ARTS-II sub-study analysis[33] reported that, at 5-year follow up, CABG has comparable safety and superior efficacy in terms of reducing repeat revascularisation compared to BMS and DES in the treatment of patients with multivessel disease involving the proximal left anterior descending artery. However, the authors concluded that appropriate patient selection remains imperative.

Coronary main stem disease

CABG is conventionally considered to be the standard therapeutic strategy in patients with significant main stem disease who are eligible for surgery, and the CASS registry reported a mean survival advantage of 7 years in 912 patients who were treated with CABG versus medication.[34] However, the latest data from the large SYNTAX trial,[35] two more recent RCTs[36,37] and a meta-analysis,[38] indicate that PCI offers equivalent results to CABG, at least in more simple lesions. None of these trials showed significant mortality differences between the two revascularisation strategies, making PCI an option for those patients unwilling to undergo surgery and prepared to accept further interventional procedures as necessary.

Subgroup analysis of the SYNTAX trial in 705 randomised patients with main stem disease indicated that 1-year rates of death (4.4% vs. 4.2%, $p=0.88$), stroke (2.7% vs. 0.3%, $p=0.009$), myocardial infarction (4.1% vs. 4.3%, $p=0.97$), repeat revascularisation (6.7% vs. 12%, $p=0.02$), and MACE (13.6% vs. 15.8%, $p=0.44$) were in favour of CABG only as regards repeat revascularisation, but with a greater risk of stroke.

Based on the tertiles of the SYNTAX score, the rates of MACE were 13% versus 7.7% ($p=0.019$), 15.5% versus 12.6% ($p=0.54$), and 12.9% versus 25.3% ($p=0.08$) for CABG and PCI, in the low (0-22), intermediate (23-32) and high (≥33) tertiles, respectively.

At 2 years, the respective death rates in the CABG group compared to the PCI group were 7.9% versus 2.7% ($p=0.02$), and the rates of repeat revascularisation were 11.4% versus 13.3% ($p=0.44$) in the two lowest tertiles, suggesting that PCI was superior to CABG. It should be noted that, of the 1212 patients with main branch disease who were included in the registry or the randomised trial, 65% had SYNTAX scores ≥33. At the Transcatheter Cardiovascular Therapeutics Congress in 2010 in Washington, Patrick Serruys from the Erasmus Medical Centre in Holland presented the results of the SYNTAX study at three years' follow up of patients with main stem disease, based on the SYNTAX score. According to these results, a SYNTAX score ≤22 is associated with higher total rates of MACE in patients in the CABG group compared to PCI (23% vs. 18%, $p=0.33$). Thorough analysis revealed higher rates of death (6% vs. 2.6%), stroke (4.1% vs. 0.9%) and composite safety endpoint (death/infarction/stroke) (11% vs. 6.9%) in the CABG group, but more myo-

cardial infarctions (4.3% vs. 2%) and repeat revascularisations (15.4% vs. 13.4%) in the PCI patients. However, none of the comparisons reached the statistical significance that had been observed at 2-year follow up, where the death rate was significantly higher in the CABG group (7.9% vs. 2.7%, p=0.02), whereas the rate of repeat revascularisation did not differ significantly (11.4% vs. 14.3%, p=0.44) in patients with a low or intermediate SYNTAX score.

Patients with an intermediate SYNTAX score had exactly the same rate of MACE (23.4%, p=0.90). The study investigators were surprised to find a 12.4% death rate for CABG compared to 4.9% for PCI (p=0.06) in this category of patients. Stroke (2.3% vs. 1%) and composite safety endpoint (death/infarction/stroke) (15.6% vs. 10.8%) were also higher in the CABG than in the PCI group. Only myocardial infarctions (3.3% vs. 5%) and repeat revascularisations (14% vs. 15.9%) were in favour of CABG. Once again, none of the comparisons reached statistical significance.

However, a SYNTAX score ≥33 was associated with a MACE rate of 37.3% in the PCI group compared to 21.2% for CABG (p=0.003). There is a gap of 16 percentage points for PCI regarding MACE. Here there is no doubt as to which strategy is better.

In addition, the death rates for PCI were almost double those for CABG (13.4% vs. 7.6%, p=0.10). Apart from stroke (4.9% vs. 1.6%, p=0.13), the rates of myocardial infarction (6.1% vs. 10.9%, p=0.18), repeat revascularisation (9.2% vs. 27.7%, p<0.001) and the composite of death/infarction/stroke (15.7% vs. 20.1%, p=0.34) were lower in the CABG than in the PCI group.

From the above data we see that PCI can be a reasonable alternative to CABG in patients with main stem disease and low or intermediate SYNTAX scores.[39]

In a meta-analysis of 10 studies,[38] including 2 RCTs and the large MAIN-COMPARE registry, incorporating 3773 patients with main stem disease, Naik et al reported that, although there was no difference between PCI and CABG as regards mortality or the composite endpoint of death, myocardial infarction and stroke at 3 years, PCI had as much as a fourfold greater rate of repeat revascularisations. Similarly, in another meta-analysis of 2 RCTs and 6 observational studies that compared DES with CABG in 2905 patients with unprotected main stem disease, no difference was found in death or in the composite endpoint of myocardial infarction and stroke, but only a significantly higher rate of repeat revascularisations in the PCI arm,[40] over a medium-term follow up. Finally, in a more recent meta-analysis[41] of all four available RCTs in 1611 patients, PCI was associated with a non-significantly higher 1-year rate of MACE (death, myocardial infarction, stroke, repeat revascularisation) compared with CABG (14.5% vs.11.8%; odds ratio, OR 1.28, 95% CI: 0.95-1.72; p=0.11), driven by increased target vessel revascularisation (11.4% vs. 5.4%; OR 2.25, 95% CI: 1.54 to 3.29; p<0.001). Conversely, stroke occurred less frequently with PCI (0.1% vs. 1.7%; OR 0.15, 95% CI: 0.03-0.67; p=0.013). There were no significant differences in death (3.0% vs. 4.1%; OR 0.74, 95% CI: 0.43-1.29; p=0.29) or myocardial infarction (2.8% vs. 2.9%; OR 0.98, 95% CI: 0.54-1.78; p=0.95).

Current guidelines recommend PCI of the left main coronary artery as a Class IIa or IIb alternative to CABG in patients who have conditions that are associated with a low risk of PCI procedural complications and/or an increased risk of adverse surgical outcomes. Based on the available data, and especially the two more recent RCTs, it is anticipated that there will be a revision of the guidelines, raising the level of evidence of the current recommendations from B to A.

Recent ESC guidelines

In patients with chronic stable CAD the choice of the most appropriate therapeutic strategy should be the result of two components:[42]

1. Eligibility for revascularisation (Table 1).
2. Relative advantages of CABG and PCI in the various anatomical and clinical forms of the disease (Table 2).

The findings we have to hand show that revascularisation is chosen:

- *On an symptomatic basis:* in patients with persistent symptoms (angina or equivalent) despite OMT, and/or
- *On a prognostic basis:* in specific anatomical forms of the disease or if there is a confirmed significant myocardial mass at risk (even in asymptomatic patients). Significant main stem disease and/or significant disease of the proximal part of the anterior descending artery, especially in the presence of multi-vessel CAD, are strong indications for revascularisation. In the more severe forms of stable CAD, CABG appears to offer a survival benefit as well as a significant reduction in the need for repeat revascularisation, despite the greater risk of stroke, especially in main stem disease.

Table 1. Indications for revascularization in stable CAD and silent ischaemia with prognostic and/or symptomatic benefit.

	Anatomical subgroup of CAD	Class	Level of evidence
Prognosis	Main stem >50%	I	A
	Proximal LAD >50%	I	A
	2-VD or 3-VD with ↓EF	I	B
	Confirmed large ischaemic region (>10% of left ventricle)	I	B
	Sole patent vessel with stenosis >50%	I	C
	1-VD without proximal LAD and without ischaemia >10%	III	A
Symptoms	Any stenosis >50% with angina or its equivalent that does not respond to optimal drug therapy	I	A
	Dyspnoea/CHF and ischaemia/viability >10% of the left ventricle from an artery with stenosis >50%	IIa	B
	Without restrictive symptoms with optimal drug therapy	III	C

CAD – coronary artery disease; LAD – left anterior descending artery; VD – vessel disease; EF – ejection fraction; CHF – congestive heart failure.

Table 2. Indications for coronary artery bypass grafting (CABG) versus percutaneous coronary intervention (PCI) in stable patients with lesions eligible for both procedures and low predicted operative mortality.

Anatomical subgroup of CAD	Pro CABG	Pro PCI
1-VD or 2-VD without proximal LAD	IIb C	IC
1-VD or 2-VD with proximal LAD	IA	IIa B
3-VD simple lesions, full revascularisation with PCI. SYNTAX score ≤22	IA	IIa B
3-VD complex lesions, incomplete revascularisation with PCI. SYNTAX score >22	IA	III A
Main stem disease, isolated or 1-VD, ostial/body	IA	IIa B
Main stem disease, isolated or 1-VD, distal bifurcation	IA	IIb B
Main stem disease + 2-VD or 3-VD, SYNTAX score ≤32	IA	IIb B
Main stem disease + 2-VD or 3-VD, SYNTAX score >32	IA	III B

Abbreviations as in Table 1.

Conclusions

In patients with chronic stable CAD, OMT is the first-line treatment and should include all necessary ingredients in doses that can achieve the therapeutic goals.

Revascularisation should always be used in conjunction with OMT and lifestyle modification and not as an alternative strategy.

In selected patients, revascularisation is effective for the control of symptoms and/or in optimising the prognosis.

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