

## REVIEW ARTICLE

# Key messages and critical approach of the 2024 guidelines of the European Society of Cardiology on chronic coronary syndromes

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## ABSTRACT

The updated European Society of Cardiology (ESC) guidelines empower physicians to tailor treatment plans more effectively to individual patient characteristics, preferences, and responses. With a more flexible and individualized approach to angina management, it seems that the traditional stepwise approach may not be optimal for all patients. In addition, there is a significant shift in the diagnostic approach for chronic coronary syndromes (CCS). In this review, we mainly refer to key points and queries concerning the current ESC recommendations regarding the diagnostic approach and treatment of patients with stable angina, recommending practical directions to physicians managing patients with CCS. (Hellenic Journal of Cardiology 2025;■:■-■) © 2025 Hellenic Society of Cardiology. Publishing services by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

## 1. INTRODUCTION

The recent update to the European Society of Cardiology (ESC) 2024 Guidelines on Chronic Coronary Syndromes (CCS) marks a significant shift in the diagnostic approach and management of CCS. The new guidelines recommend three main steps for the evaluation of patients suspected of CCS. The first emphasizes the importance of accurate assessment of symptoms and signs, the second recommends a thorough cardiac examination with echocardiography (ECG), and the third discusses other diagnostic tests to establish the diagnosis.

The previous recommendation positioned nicorandil, ranolazine, ivabradine, and trimetazidine as

second-line treatments to be considered only after  $\beta$ -blockers, calcium channel blockers (CCBs), and long-acting nitrates had been tried or excluded because of intolerance or contraindications. In contrast, the revised guidelines acknowledge that there are no studies to support the superiority of any antianginal over another. Long-acting nitrates and ranolazine are recommended as add-on therapy in patients on  $\beta$ -blockers and/or CCBs with inadequate symptom control or even as part of initial treatment in select patients. This change reflects a more flexible and individualized approach to angina management, acknowledging that the traditional stepwise approach may not be optimal for all patients. Notably, the revision challenges the previous hierarchical

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treatment structure by removing the strict requirement for first-line therapies to have failed or be unsuitable for patients before considering alternative medications. The guideline update thus allows for earlier consideration of agents previously considered second-line in the treatment algorithm, potentially benefiting patients who might respond well to these medications regardless of their experience with other antianginal drugs. This more nuanced approach to pharmacological management of angina symptoms underscores the complexity of treating CCS and the need for personalized treatment strategies.

In this review, we mainly refer to key points and queries concerning the current ESC guidelines for the diagnostic approach and treatment of patients with stable angina, recommend practical directions to physicians managing patients with CCS.

## 2. APPROACH TO THE DIAGNOSIS OF PATIENTS WITH SUSPECTED CCS

The new, recently published ESC guidelines<sup>1</sup> on the management of CCS have made some significant changes from the ESC guidelines published in 2019. The new guidelines recommend three main steps for the evaluation of patients suspected with CCS. The first emphasizes the importance of accurate assessment of symptoms and signs to enhance the likelihood of correct diagnosis and determining the etiology of the condition. The second includes cardiac examination with ECG and a tool to estimate the clinical likelihood of obstructive coronary artery disease (CAD). The third step discusses diagnostic testing to establish the diagnosis.

A significant focus of the third step is avoiding invasive coronary arteriography (ICA), which is reserved only for potential cases of the most significant form of obstructive CAD. Although the guidelines state that a large number of patients with anginal chest pain will have non-obstructive disease and/or microvascular dysfunction, it emphasizes the focus on diagnosing obstructive CAD. However, the importance of these aspects is covered by other sections of the guidelines in greater detail. The fourth step deals with lifestyle and risk factor modification and symptomatic treatment of anginal symptoms with antianginal medication. Revascularization is reserved only for those patients whose symptoms persist despite medical treatment.

The revised guidelines rationalize using ECG testing as a low cost, widely accessible non-radiation-based evaluation, which remains an alternative for diagnostic testing, emphasizing the importance of available local resources and individual

characteristics. The graded exercise ECG can reveal limiting chest pain or discomfort, significant ischemic ECG changes, arrhythmias, excessive hypertension, and hypotension and has been one of the mainstays of evaluation techniques used in clinical cardiology for assessing individuals with suspected CCS. The guidelines emphasize the limitations of this test, which has a lower diagnostic capability of identifying obstructive CAD than modern functional imaging and coronary computed tomography angiography (CCTA). Therefore, the guidelines recommend that modern functional imaging and CCTA are preferred as first-line tests in subjects with suspected CCS, depending on availability and local experience. The guidelines provide evidence to support a strategy based on anatomical<sup>2-5</sup> or functional imaging<sup>6</sup> that simplifies the diagnosis, enables the targeting of preventive therapies and interventions, and potentially reduces the risk of the myocardial infarction (MI) compared with usual care based on exercise ECG. Additional evidence supports that patients randomized to CCTA instead of exercise ECG as an index investigation for stable chest pain report fewer anginal complaints during follow-up.<sup>3,7</sup>

In the new guidelines, anatomical imaging is discussed, and it is recommended that CCTA is utilized instead of ICA. CCTA allows direct anatomical visualization of the coronary artery lumen and wall. Compared with ICA, CCTA offers a practical, non-invasive test with proven diagnostic performance in detecting obstructive coronary artery stenosis.<sup>8,9</sup>

The 2024 guidelines emphasize that intermediate stenosis may not be hemodynamically or functionally significant<sup>10</sup> or induce myocardial ischemia.<sup>11</sup> Depending on the clinical context, it may be necessary to complement CCTA with functional data either from non-invasive imaging techniques or from invasive angiography with fractional flow reserve (FFR). Coronary computed tomography (CT) angiography-derived fractional flow reserve (FFR-CT) can complement CCTA by providing values of model-based computational FFR along the coronary tree. The guidelines also give recommendations for when CCTA is not recommended in patients.

The revised guidelines support CT perfusion imaging performed under pharmacological stress and provide evidence that this technique has been validated against several reference standards, including single-photon emission CT (SPECT) and invasive FFR. CT perfusion imaging shows adequate diagnostic performance in select cohorts<sup>12,13</sup> and a potential to reduce the number of unnecessary downstream invasive angiography procedures compared with functional tests (mostly symptom-limited exercise

ECG).<sup>14</sup> Although CT perfusion imaging can complement CCTA during the same visit, this technique requires the administration of a pharmacological stressor, contrast agent, and further patient irradiation. The guidelines also note that imaging techniques and analysis methods are not yet widely standardized (e.g., static and dynamic imaging techniques and visual and quantitative assessment).<sup>15-17</sup>

Most of the recommendations for the evaluation of the majority (85%) of patients with suspected CCS are for non-invasive assessment rather than recommendation of invasive investigation (Table 1).

### 3. THERAPEUTIC APPROACH IN PATIENTS WITH CCS

Treatment involves lifestyle changes and medication. In all patients, lifestyle modification, statins, renin-angiotensin-aldosterone system (RAAS) inhibitors, and antiplatelet agents are the only interventions that increase survival. Antianginal medications including  $\beta$ -blockers, CCBs, nitrates, ranolazine, ivabradine, nicorandil, and trimetazidine are used to improve symptoms.

**3.1. LIFESTYLE CHANGE.** Both ESC<sup>1</sup> and ACC/AHA guidelines<sup>18</sup> agree that in addition to any pharmaceutical or invasive treatment, lifestyle change plays an important role.

**3.2. MEDICAL TREATMENT.** Regarding mortality, MI, and other major adverse cardiovascular events, several studies and meta-analyses<sup>19,20</sup> have unequivocally shown that in subjects with stable angina pectoris, there is no superiority of interventional therapy compared to medical treatment. The ESC guidelines<sup>1</sup> recommend that patients with stable angina pectoris should start with non-invasive diagnostic methods and medications, and if angina pectoris persists, treating physicians should consider invasive management.

**Critical approach:** According to the recommendations and scientific documentation supporting the current ESC guidelines,<sup>1</sup> no studies that directly compared various antianginal drugs have demonstrated the superiority of one group over another.<sup>1</sup> There are also no randomized controlled trials showing that older drugs ( $\beta$ -blockers, nitrates, calcium antagonists, trimetazidine) are superior to newer drugs (ranolazine, ivabradine, nicorandil).<sup>1</sup> In addition, no antianginal drug has shown improvement in survival other than  $\beta$ -blockers in patients after MI and low ejection fraction (EF).<sup>1</sup>

In recent years, several publications analyzing both the 2013 and 2019 guidelines for managing patients with stable angina have challenged the conventional stepwise approach and proposed a more individualized treatment strategy, arguing that therapy should be primarily guided by the patient's blood pressure and heart rate levels while taking into account any coexisting medical conditions. This approach emphasizes tailoring treatment to each patient's specific physiological parameters and overall health status rather than following a predetermined sequence of interventions (Fig. 1).<sup>21-24</sup> The latest guidelines adopt the "diamond approach" for choosing the antianginal drug combination according to patient's heart rate, blood pressure, and comorbidities. Curiously, they still recommend some pharmacotherapy as a priority over other treatments, also suggesting the stepwise approach.

**$\beta$ -blockers** are recommended as the first choice in patients with stable angina pectoris with an indication I B. As mentioned in the guideline text,<sup>1</sup> there is no evidence showing a benefit of their use in patients without a previous MI and preserved EF.

**Critical approach:** One issue that needs to be clarified is how long patients should take  $\beta$ -blockers after an acute coronary syndrome. Guidelines from the ACC/AHA<sup>18</sup> recommend that in patients with

**TABLE 1** Main chronic coronary syndromes symptoms and diagnostic approach

|   |         |                                     |
|---|---------|-------------------------------------|
| Step 1  |         |                                     |
| Symptoms: Chest discomfort and Dyspnoea                                 |         |                                     |
| Step 2  |         |                                     |
| Estimation of clinical likelihood                                       |         |                                     |
| Step 3  |         |                                     |
| Estimation of risk factors and risk factor-weighted clinical likelihood |         |                                     |
| Step 4  |         |                                     |
| Diagnostic test—Clinical likelihood                                     |         |                                     |
| Very low  | <5%     | Defer further testing               |
| Low   | >5-15%  | ECG, echo or CCTA                   |
| Moderate  | >15-50% | CCTA or PET/SPECT, CMR, stress echo |
| High  | >50-85% | PET/SPECT, CMR, stress echo         |
| Very high   | >85%    | ICA                                 |

**FIGURE 1** Individualize treatment according patients hemodynamic parameters and comorbidities. Class of recommendation is according ESC guidelines 1

### Individualize treatment according patients hemodynamic parameters and comorbidities

| AV conduction abnormalities   | Atrial fibrillation/flutter   | Microvascular angina   | Vasospastic angina  | HFrEF   | Diabetes melitus  | Pulmonary disease   |
|---|---|--|---|---|---|---|
| Dihydropyridine CCB IB<br>Nitrates IIa<br>Nicorandil IIb<br>Ranolazine IIa<br>Trimetazidine IIb | beta blockers IB<br>Dihydropyridine CCB IB<br>Diltiazem IB<br>Ranolazine IIa<br>Nitrates IIa<br>Nicorandil IIb<br>Trimetazidine<br>Verapamil IB | beta blockers IB<br>Dihydropyridine CCB IB<br>Non Dihydropyridine CCB IB<br>Ivabradine *IIa<br>Ranolazine IIa<br>Trimetazidine IIb | Dihydropyridine CCB IB<br>Diltiazem IB<br>Ivabradine * IIa<br>Nitrates IIa<br>Ranolazine IIa<br>Trimetazidine IIb<br>Verapamil IB | b blockers IB<br>Ivabradine *IIa<br>Nitrates IIa<br>Nicorandil IIb<br>Ranolazine IIa<br>Trimetazidine IIb | Vasodilating b blockers IB<br>Dihydropyridine CCB IB<br>Diltiazem IB<br>Ivabradine * IIa<br>Nitrates IIa<br>Nicorandil IIb<br>Ranolazine IIa<br>Trimetazidine IIb<br>Verapamil IB | Cardio selective beta blockers IB<br>Dihydropyridine CCB IB<br>Diltiazem IB<br>Ivabradine *IIa<br>Nitrates IIa<br>Nicorandil IIb<br>Ranolazine IIa<br>Trimetazidine IIb<br>Verapamil IB |
| SBP<120 mmHg  |   | SBP>120 mmHg   |   | HR < 60 bpm   |   | HR > 60 bpm   |
| Ranolazine<br>Ivabradine *<br>Trimetazidine   |   | ALL  |   | Nitrates<br>Nicorandil<br>Trimetazidine<br>Ranolazine   |   | ALL   |

CCB: Calcium channel blockers, HFrEF: heart failure with reduced ejection fraction. \* Ejection fraction  $\leq$  40%, Heart rate  $\geq$  70 bpm.

EF <40% with or without MI, their use is beneficial. In patients taking  $\beta$ -blockers with MI and EF < 50%, if there is no other indication (arrhythmia, hypertension, etc.), their use after one year should be re-evaluated. If the patient does not have a previous MI or has EF <50%, their use is not beneficial.

At this point, we would like to comment on the following. Previous studies affirmed that in previous guidelines, indication I A of the recommendation to administer  $\beta$ -blockers in patients with stable angina was inappropriate because there are no studies to validate this recommendation.<sup>21-24</sup> In the current ESC guidelines, the indication was downgraded from I A to I B without a comment in the text that analyzes the new changes (mentioned at the beginning of the manuscript). It is also surprising that there is a persistence in recommending starting with  $\beta$ -blockers when there is no evidence to support this, as the authors state in the text of the guidelines. In addition, in recent studies such as the REDUCE-AMI<sup>25</sup> that enrolled patients with MI and EF > 50%, long-term  $\beta$ -blocker treatment did not improve cardiovascular morbidity or mortality, whereas the ABYSS trial<sup>26</sup> showed that in patients with a history of MI, interruption of long-term  $\beta$ -blocker treatment had the same results. Moreover, all studies with  $\beta$ -blockers used to formulate the current guidelines are studies

from 1980 to 1990, before the arrival of statins, RAAS inhibitors, and antiplatelet agents,<sup>21-24</sup> medications that significantly improve the prognosis of these patients. Finally, the majority of these studies had very small numbers of patients than the more recent studies, and this is also true for the studies involving nitrates and CCBs.<sup>21-24</sup>

In the new guidelines, non-dihydropyridine calcium antagonists are recommended as an alternative if  $\beta$ -blockers cannot be used and heart rate reduction is required.

**3.2.1. Combination treatment.** In the new guidelines, it is suggested that medical treatment decisions should take into account the patient's hemodynamic profile and comorbidities.<sup>1</sup> If there is no contraindication, combination therapy with  $\beta$ -blockers and CCBs is recommended as the first choice for patients whose symptoms are not controlled.<sup>1</sup>

**Critical approach:** Although in daily clinical practice this combination is effective, there are no published studies affirming that the combination of these agents reduces symptoms or improves exercise time, and there are no comparative studies with other drugs. In addition, when combining these two agents, blood pressure should be considered; in patients with CAD, it should not be less than <120/70 mmHg.<sup>21-24</sup> There are studies of combination treatment with

**TABLE 2 Medical treatment for chronic coronary syndromes (Main messages) Antianginal and Antithrombotics**

|   |       |
|---|-------|
| 1. It is recommended to tailor the selection of antianginal drugs to the patients characteristics, comorbidities, concomitant medications, pathophysiology of angina etc.   | I C   |
| 2. Initial treatment with b-blockers and/or CCB to control heart rate and symptoms for most patients  | I B   |
| 3. If anginal symptoms are not successfully controlled with a b-blocker or a CCB their combination should be considered   | Ila B |
| 4. Long acting nitrates or ranolazine should be considered as add-on therapy in patients with inadequate control of symptoms while on treatment with b-blocker and/or CCB in properly selected patients                 | Ila B |
| 5. Ivabradine should be considered as add-on therapy in patients with LVEF < 40% and inadequate control of symptoms or as part of initial treatment in selected patients  | Ila B |
| 6. Nicorandil or trimetazidine may be considered as add-on therapy in patients with inadequate control of symptoms while on treatment with b-blockers and/or CCB or as a part of initial treatment in selected patients | Ilb B |
| 7. Ivabradine is not recommended as add-on therapy in patients with LVEF > 40% and no clinical heart failure  | III B |
| 8. In CCS patients with atherosclerotic CCS, low dose colchicine (0.5 mg daily) should be considered to reduce myocardial infarction, stroke, and need for revascularization  | Ila A |
| 9. Lipid lowering treatment with high intensity treatment with LDL-C goal of <1.4 mmol/L (55 mg/dL) and a >50% reduction in LDL-C vs baseline is recommended  | I A   |
| If a patients goal is not achieved with the maximum tolerated dose of statin, combination with ezetimide is recommended   | I B   |
| For patients who do not achieve their goal on a maximum tolerated dose of statin and ezetimide combination with a PCSK9 inhibitor is recommended  | I A   |
| 10. SGLT2 inhibitors are recommended in patients with T2DM and CCs independent of HbA1C   | I A   |
| 11. GLP-1 receptor agonists are recommended in patients with T2DM and CCS independent of HbA1C  | I A   |
| 12. In patients without prior MI or revascularization but with evidence of significant CAD, aspirin 75-100 mg daily is recommended life long.   | I B   |
| 13. In CCS patients with a prior MI or remote PCI aspirin 75-100 mg daily or clopidogrel 75 mg daily is recommended as alternative to aspirin after initial period of DAPT  | I A   |
| 14. A proton pump inhibitor is recommended in patients at increased risk of gastrointestinal bleeding for the duration of combined antithrombotic therapy   | I A   |

newer antianginal drugs showing that the combination of a  $\beta$ -blocker with ivabradine (if heart rate is >70 bpm) or with ranolazine is effective regardless of heart rate (ranolazine) and blood pressure (ranolazine, ivabradine).<sup>21-24</sup> Thus, there is no evidence supporting the combination of  $\beta$ -blocker with CCBs (first choice) is superior than the combination of a  $\beta$ -blocker with ivabradine or ranolazine (not first choice).

**3.2.2. Nitrates.** The inclusion of long-acting nitrates with ranolazine as potential add-ons or initial therapies introduces an important caveat.

Critical approach: Although long-acting nitrates have been a mainstay of angina treatment for decades, recent research has raised concerns about their long-term effects on patient outcomes. The updated guidelines implicitly acknowledge the ongoing debate surrounding the use of long-acting nitrates by placing them on par with ranolazine, a relatively newer agent with a different mechanism of action. This juxtaposition is particularly noteworthy given the emerging evidence suggesting that long-acting nitrates may have a detrimental effect on prognosis in some patients with CCS. The guidelines' new formulation thus encourages clinicians to carefully weigh the potential symptomatic benefits of long-acting nitrates against their possible negative impact on long-term outcomes. They are suggested as an alternative, in combination with a  $\beta$ -blocker, but there are no studies showing that

their addition improves exercise time; a recent study showed no difference between placebo and nitrates in patients with stable angina.<sup>27</sup> There are also studies affirming that the long-term use of nitrates can cause endothelial dysfunction or increase oxidative stress.<sup>28,29</sup> Moreover, we should not forget the issue of tolerance and the risk of hypotension. Finally, all the studies cited in current guidelines are 30-40 years old and based on a small number of patients.

**3.2.3. Ranolazine.** This agent is upgraded from previous guidelines to the same level as nitrates. There are many studies and meta-analyses that have shown that ranolazine as monotherapy or combination therapy increases exercise time and decreases nitrate utilization without affecting heart rate and blood pressure.<sup>21-24</sup> Studies and meta-analyses have shown that it also has pleiotropic effects because it reduces HbA1C and the new onset of atrial fibrillation and ventricular tachycardia and is effective for microvascular angina pectoris.<sup>21-24,30</sup> Moreover, ranolazine may be considered in patients with low heart rate or low blood pressure because it does not affect these hemodynamic parameters. It is well known that in patients with CAD, the J curve phenomenon is important.<sup>31</sup> Since both drugs received the same Ila B indication in the guideline, and ranolazine has a number of beneficial pleiotropic actions, why is priority given to the use of nitrates in combined therapy?

Critical approach: Ranolazine had no effect on the primary composite endpoint of cardiovascular death, acute MI, or recurrent ischemia in the MERLIN-TIMI 36 (Metabolic Efficiency with Ranolazine for Less Ischemia in Non-ST-Elevation Acute Coronary Syndromes: Thrombolysis in Myocardial Infarction 36).<sup>32</sup> Only in the prespecified subgroup of patients with prior chronic angina, ranolazine significantly improved the primary endpoint.<sup>33</sup> In addition, in the Ranolazine in Patients with Incomplete Revascularization Percutaneous Coronary Intervention (RIVER-PCI) trial in patients with history of chronic stable angina and incomplete revascularization after PCI, ranolazine did not reduce the composite rate of ischemia-driven revascularization or ischemia-driven hospitalization without revascularization.<sup>34</sup> Moreover, the cost of ranolazine is considerably higher than that of other antianginal drugs ( $\beta$ -blockers, CCBs, nitrates) and may prolong the QT interval.

**3.2.4. Ivabradine.** In the revised guidelines, this agent is recommended as second-line treatment in patients with stable angina and EF <40%.<sup>1</sup> This restrictive recommendation was made despite the fact that in the supplement, the authors affirm that there are studies proving that ivabradine improves all exercise stress testing variables (exercise duration, anginal attacks, etc) not only in combination therapy but also as monotherapy in patients with stable angina as well as those with preserved EF. This recommendation was based on a misinterpretation of the Study Assessing the Morbidity-Mortality Benefits of the If Inhibitor Ivabradine in Patients With Coronary Artery Disease study,<sup>35</sup> which used increasing dosages of ivabradine, up to 10 mg twice daily. The study suggested the risk of events increased only in those patients co-prescribed with diltiazem or verapamil (which are contraindicated in patients receiving ivabradine and/or  $\beta$ -blockers). Ivabradine as well as ranolazine are the most well studied agents for stable angina in thousands of patients, which is not true, at least to the same extent, for other antianginal agents, even those recommended as first-line treatments.<sup>21-24</sup>

**3.2.5. Nicorandil and trimetazidine.** These drugs are recommended as add-on treatments with the aforementioned agents in patients with refractory angina. Although there are no new studies supporting it, the recommendation of these two agents was downgraded from IIa B to IIb B compared to previous guidelines. In addition, these agents may be considered for first-line treatment according to the patient's heart rate, blood pressure, and tolerance.<sup>1</sup> In the supplement of the article, it is mentioned that the

concomitant use of nicorandil with aspirin may increase the risk of gastrointestinal ulcers, perforations, and hemorrhage. It seems that the best approach before starting any treatment is to know the patient's heart rate, blood pressure, and comorbidities, and the selection of the ideal drug should be based to all of these.

Regarding the efficacy of all major antianginal drugs, it seems that no antianginal drug is superior to another.<sup>36</sup>

#### 4. LIPID PROFILE MANAGEMENT

The 2024 ESC Guidelines on CCS represent a significant evolution in the approach to lipid management for patients with CCS. The previous guidelines simply recommended statins for all CCS patients, without specifying intensity or target levels. In contrast, the new guidelines provide a more nuanced, aggressive, and patient-centered approach to lipid-lowering therapy.<sup>1</sup>

The updated recommendations emphasize the use of high-intensity statins at the maximum tolerated dose for all CCS patients. This shift reflects the growing body of evidence supporting the benefits of more intensive statin therapy in reducing cardiovascular risk. By specifying "high-intensity" statins, the guidelines encourage the use of more potent medications such as atorvastatin or rosuvastatin at higher doses, which have been shown to provide greater reductions in low-density lipoprotein cholesterol (LDL-C) and improved cardiovascular outcomes.<sup>1</sup>

Furthermore, the new guidelines set clear and ambitious targets for LDL-C reduction. The primary goal is to lower LDL-C levels below 1.4 mmol/L (55 mg/dL) and achieve at least a 50% reduction from baseline. These targets are more aggressive than previous recommendations and align with the classification of CCS patients as being at very high cardiovascular risk. This risk stratification acknowledges the substantial ongoing risk of cardiovascular events in patients with established CAD, even when traditional risk factors are well-controlled.

The guideline also introduces a tiered approach to LDL-C management by suggesting an even lower target of <1.0 mmol/L (40 mg/dL) for patients who experience a second vascular event within two years' despite being on maximum tolerated statin therapy.<sup>1</sup> This recommendation recognizes the heterogeneity within the CCS population and the need for more intensive treatment in those with recurrent events or particularly high-risk profiles. It also reflects the growing understanding that some patients may benefit from LDL-C levels well below traditional targets.

This updated approach aligns with the “lower is better” paradigm for LDL-C management that has emerged from recent clinical trials. It also implicitly acknowledges that statins alone may not be sufficient to achieve these ambitious targets in all patients, potentially paving the way for increased use of non-statin lipid-lowering therapies such as ezetimibe or PCSK9 inhibitors in combination with high-intensity statins.

## 5. THE ROLE OF INFLAMMATION IN ATHEROSCLEROSIS

The inclusion of low-dose colchicine as a recommended therapy for patients with CCS in the ESC 2024 Guidelines marks a significant shift in the management of atherosclerotic CAD. This new recommendation reflects the growing recognition of inflammation's role in atherosclerosis and represents an innovative approach to reducing cardiovascular risk beyond traditional lipid-lowering and anti-thrombotic strategies.

The recommendation is primarily based on the results of two landmark trials: COLCOT (Colchicine Cardiovascular Outcomes Trial)<sup>37</sup> and LoDoCo2 (Low-Dose Colchicine 2),<sup>38</sup> as well as a meta-analysis encompassing over 12,000 patients with atherothrombotic CAD.<sup>39</sup> These studies consistently demonstrated that low-dose colchicine (0.5 mg daily) significantly reduced the risk of major adverse cardiovascular events, including MI, stroke, and the need for revascularization.

**Critical approach:** The revised recommendation also raises important considerations. The long-term safety and efficacy of colchicine in this population need to be carefully monitored, as the available trials have relatively short follow-up periods. Additionally, the optimal patient selection for colchicine therapy and its interaction with other cardiovascular medications require further study.

A summary of the main messages and changes of medical treatment is shown in [Table 2](#).

## 6. CORONARY REVASCLARIZATION

The Guidelines' recommendations on the decision-making process for coronary revascularization reflect a significant emphasis on patient-centered care, shared decision making, and multidisciplinary collaboration.<sup>1</sup> This approach represents a notable evolution in the management of complex CAD cases.

The guidelines strongly emphasize the importance of providing patients with comprehensive

information about their treatment options. This includes not only the benefits and risks of revascularization but also the therapeutic consequences and alternatives. By recommending this level of detail in patient communication, the guidelines aim to empower patients to make informed decisions about their care, aligning with the principles of patient autonomy and shared decision making.

The recommendation for a Heart Team discussion in complex cases, particularly when coronary artery bypass grafting and PCI are equally appropriate, underscores the value of multidisciplinary expertise in tailoring treatment strategies. This approach ensures that patients benefit from collective wisdom that spans different specialties, potentially leading to more nuanced and personalized treatment plans.

The guidelines' emphasis on communicating the Heart Team's proposal in a balanced and understandable manner is crucial. It recognizes the potential for medical jargon to create barriers in patient understanding and decision making.

The recommendation to consider patient preferences, health literacy, cultural circumstances, and social support in the decision-making process is particularly noteworthy. This patient-centered approach acknowledges that medical decisions do not occur in a vacuum but are influenced by a patient's individual context and values.

The final recommendation for Heart Teams to develop institutional protocols for implementing appropriate revascularization strategies in accordance with current guidelines is an important step toward standardizing care while allowing for institutional flexibility. This approach can help ensure that evidence-based practices are consistently applied across different health care settings, potentially reducing unwarranted variations in care.

Overall, these recommendations represent a shift toward a more collaborative, patient-centered, and standardized approach to decision making in coronary revascularization. They reflect an understanding that optimal outcomes in complex cardiac cases require not only technical expertise but also effective communication, patient engagement, and multidisciplinary collaboration. This approach has the potential to improve not only clinical outcomes but also patient satisfaction and quality of life.

## 7. CONCLUSIONS

By broadening the options for initial and add-on therapies, the updated guidelines empower

physicians to tailor treatment plans more effectively to individual patient characteristics, preferences, and responses. This shift may lead to improved symptom control and quality of life for patients with chronic angina while potentially mitigating the risks associated with long-term use of certain medications. The revision also highlights the dynamic nature of medical guidelines, reflecting the ongoing evolution of clinical evidence and expert consensus in the field of cardiovascular medicine.

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## CONFLICT OF INTEREST

There is nothing to declare in relation to this manuscript.

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