

# New 2024 European Society of Cardiology Guidelines for the Management of Chronic Coronary Syndromes. Highlights and Comparison with Other Clinical Practice Guidelines

*Nueva guía europea de síndromes coronarios crónicos 2024. Aspectos destacados y comparación con otras guías de práctica clínica*

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The new 2024 European Society of Cardiology (ESC) clinical practice guidelines (CPG) for the management of chronic coronary syndromes (CCS) (1) revise the previous 2019 version (2) and the 2018 myocardial revascularization guidelines, (3) so that they serve as a double document. Their analysis is relevant as they are the first CPG on chronic coronary artery disease (CAD) developed by the ESC published after the IS-CHEMIA study (4) appeared in 2020. This document involves professionals from 41 countries in Europe and is endorsed by the European Association for Cardio-Thoracic Surgery. The process of voting and approval of the recommendations requires an agreement from at least 75% of the members. Following multiple rounds of double-blind peer review by external experts, the guidelines are signed off by all the experts in the Task Force for their publication.

The aim of this article is to highlight the state-of-the-art in CCS and compare the selected classes of recommendations (COR) and levels of evidence (LOE) with the previous versions of the guidelines developed by the ESC, American Heart Association (AHA) and American College of Cardiology (ACC).

## NEW DEFINITION

"CCS are a range of clinical presentations or syndromes that arise due to structural and/or functional alterations related to chronic diseases of the coronary arteries and/or microcirculation. These alterations can lead to transient, reversible, myocardial demand vs. blood supply mismatch resulting in hypoperfusion (ischemia), usually (but not always) provoked by exertion, emotion or other stress, and may manifest as angina, other chest discomfort, or dyspnea, or be asymptomatic. Although stable for long periods, chronic coronary artery diseases are frequently progressive and may

*destabilize at any moment with the development of an ACS*".

The 2024 definition differs from the previous one in the emphasis on functional alterations and microcirculation, which has been discussed in a section dedicated to INOCA/ANOCA (ischemia/angina with non-obstructive coronary arteries). Accordingly, from a pathophysiologic perspective, the CCS umbrella encompasses macrovascular and microvascular alterations, and, from the clinical point of view, the following five scenarios:

1. The symptomatic patient with reproducible stress-induced angina or ischemia with epicardial obstructive CAD.
2. The patient with angina or ischemia caused by epicardial vasomotor abnormalities or functional/structural microvascular alterations in the absence of epicardial obstructive CAD (ANOCA/INOCA).
3. The non-acute patient post-ACS or after a revascularization procedure.
4. The non-acute patient with heart failure (HF) of ischemic or cardiometabolic origin.
5. The asymptomatic patient in whom epicardial CAD is detected during an imaging test for refining cardiovascular risk assessment.

These five scenarios are identical to those used by the 2023AHA/ACC CPG for the management of chronic CAD. (5)

Like the 2019 ESC CPG, this document involves the use of steps, in this case four (instead of six), to describe the patient evaluation process: general clinical examination, further evaluation, confirming diagnosis and initial treatment, followed by pharmacologic treatment and revascularization.

The second step, called "further evaluation", introduces one of the greatest and most controversial

ARGENT J CARDIOL 2024;92:434-437. <http://dx.doi.org/10.7775/rac.v92.i6.20835>

Received: 10/02/2024 – Accepted: 12/03/2024

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changes; the risk factor-weighted clinical likelihood (RF-CL) model derived from the publication by Winther et al. (6) The document defends this model because it is patient-centered and accurate compared with more advanced models requiring computed calculation, and categorizes three times more subjects as being at very low risk compared with the 2019 CPG. This model includes sex, age, symptoms (chest pain and/or dyspnea) and risk factors (family history, smoking, dyslipidemia, hypertension and diabetes). Thus, the estimated pretest likelihood values range from 0 to 45%. The symptom score replaces the previous terminology of anginal pain symptoms (typical, atypical and non-cardiac/non-anginal), which the ESC now considers potentially misleading. Individual adjustment of the likelihood may be necessary for subjects with severe single risk factors or comorbidities such as familial hypercholesterolemia, severe renal dysfunction, rheumatic/inflammatory diseases, and peripheral vascular disease (PVD).

The CPG highlights that: *"In general, individuals with a very low ( $\leq 5\%$ ) likelihood of obstructive CAD do not require further diagnostic testing unless symptoms persist and non-cardiac causes have been excluded. In patients with a low ( $> 5\%$ - $15\%$ ) likelihood, the benefit of diagnostic testing is uncertain, but may be performed if symptoms are limiting and require clarification. Patients with moderate ( $> 15\%$ - $50\%$ ), high ( $> 50\%$ - $85\%$ ), and very high ( $> 85\%$ ) likelihood of obstructive CAD are encouraged to undergo further diagnostic testing".*

In addition, they expand the concept of RF-CL and recommend adjusting for the following six complementary clinical data or risk enhancers (COR I, LOE C): resting ECG changes, exercise ECG with abnormal findings, ventricular dysfunction, ventricular arrhythmia, acute pulmonary edema (APE), and coronary artery calcification on pre-existing computed tomography (CT) scan. In the particular case of low-risk patients (without enhancers), the CPG weight the combination of the coronary artery calcium score (CACS) with the RF-CL model, as it shows the strongest potential to defer diagnostic testing (COR IIa, LOE B) to reclassify subjects as very low likelihood of obstructive CAD.

To summarize, the maximum estimated pretest likelihood is 45%, and higher percentages can be reached with the use of risk enhancers. The difficulty arises because the CPG do not provide any tool to use risk enhancers to calculate high or very high pre-test likelihood. How can this calculation be made? The document does not provide definitive insights on this pivotal matter. Nevertheless, the following discussion on the X social media platform helps to a better understanding. In a post dated September 6, 2024, Dr. Capodanno (CPG reviewer and renowned editor-in-chief of EuroIntervention) points out this problem. Dr. Christiaan Vrints, chair of the CPG, answers: *"The idea is to make a 'clinical' judgment, not a calcula-*

*tion, based on the number and severity of the 'likelihood enhancers'. If you are convinced about 'very high' CL, go directly to invasive coronary angiography; if you estimate 'high' CL, order functional imaging."* (7) Although Dr. Vrints emphasizes that the decision is based on clinical judgment, there is a discrepancy, as the CPG suggests percentages for estimating the risk.

### CONFIRMING DIAGNOSIS

Once patient's risk has been obtained using the RF-CL model, the document suggests first-line tests and management strategies in symptomatic patients with suspected CCS:

- Very low risk ( $\leq 5\%$ ): defer further testing.
- Low risk ( $> 5\%$ - $15\%$ ): consider CACS to re-estimate the risk or coronary computed tomography angiography (CCTA).
- Moderate risk ( $> 15\%$ - $50\%$ ): CCTA or functional tests as single photon emission-computed tomography (SPECT), stress echocardiography or cardiac magnetic resonance imaging (MRI).
- High risk ( $> 50\%$ - $85\%$ ): functional test (SPECT, stress echocardiography or cardiac MRI).
- Very high risk ( $> 85\%$ ): invasive coronary angiography.

The document highlights the added value of CACS performed simultaneously with nuclear medicine imaging, e.g. PET-CT (COR I-LOE B). It also emphasizes that there is growing support for the use of CCTA as a first-line test in the low to moderate probability group ( $> 5\%$ - $50\%$ ) (COR I, LOE A), and introduces CCTA-derived fractional flow reserve (FFR-CT) as a novel approach for risk stratification in proximal left anterior descending coronary artery stenosis  $\geq 70\%$  (COR I, LOE B).

In very high-risk patients, invasive coronary angiography via the radial access (COR I, LOE A) is indicated with selective assessment of functional severity of intermediate diameter stenoses to guide the decision to revascularize, using the following tools:

- FFR or iFR (instantaneous wave-free ratio), significant with values  $\leq 0.8$  or  $\leq 0.89$ , respectively (COR I, LOE A). *A similar recommendation is provided by the 2023 AHA/ACC CPG for the management of chronic CAD.*
- QFR or quantitative flow ratio, significant with value  $\leq 0.8$  (COR I, LOE B). *Not mentioned in the 2023 AHA/ACC CPG for the management of chronic CAD.*

### TREATMENT

#### Pharmacological novelties

- The CPG propose rearranging antianginal medications, eliminating the concept of first-line or second-line drugs. Without new drugs, the document reinforces the concept that medical therapy should be tailored to each patient (COR I, LOE C).
- The recommendation to use clopidogrel as an alternative to aspirin is now stronger (COR I, LOE

A) due to its efficacy and safety. *The 2023 AHA/ACC CPG for the management of chronic CAD do not recommend it as antiplatelet monotherapy.*

In addition, two cardiometabolic drugs and one anti-inflammatory drug have been incorporated:

- Sodium glucose co-transporter 2 inhibitors for patients with diabetes (COR I, LOE A). *The same recommendation is provided by the 2023 AHA/ACC CPG for the management of chronic CAD.*
- Glucagon-like peptide-1 receptor agonists (GLP-1 RA) in patients with overweight and obesity (COR IIa, LOE B). *The 2023 AHA/ACC CPG for the management of chronic CAD have stated that there is no evidence yet to recommend these drugs in patients without diabetes.*
- Low-dose colchicine (COR IIa, LOE A). The results of the COLCOT (8) and LoDoCo2 (9) studies provided the basis for the introduction of a drug with a direct anti-inflammatory mechanism and a high level of recommendation for the treatment of chronic CAD. *For the 2023 AHA/ACC CPG for the management of chronic CAD this drug has a COR IIb, LOE B.*

#### Revascularization

Revascularization is defined by symptoms, risk and coronary anatomy, similar to the definition of the 2023 AHA/ACC CPG for the management of chronic CAD. The recommendations emphasize the participation of the Heart Team (HT). The most relevant recommendations are:

- Coronary artery bypass graft (CABG) surgery (COR I, LOE A) is recommended for patients with severe left main coronary artery (LMCA) disease, LMCA with multivessel disease (MVD) or MVD with diabetes.
- CABG surgery (COR I, LOE A) is recommended for patients with three-vessel disease and preserved left ventricular ejection fraction (LVEF). *This key point is the opposite of the 2021 ACC/AHA/SCAI Guideline for Coronary Artery Revascularization, (10) in which the recommendation was class IIb, resulting in significant controversy worldwide.* The level of disagreement was such that the American Association for Thoracic Surgery and the Society of Thoracic Surgeons withdrew from the document. Although this was amended in the 2023 AHA/ACC CPG for the management of chronic CAD with a COR IIa, LOE B, the debate continued. (11,12)
- Percutaneous coronary intervention (PCI) is recommended for LMCA disease of low complexity with a SYNTAX score  $\leq 22$  (COR I, LOE A), or as an alternative to surgery in three-vessel disease, preserved left ventricular function and absence diabetes, with a SYNTAX score  $\leq 32$  (COR I, LOE A). *Regarding this last point, the 2021 ACC/AHA/SCAI CPG also provided a low COR (IIb) versus medical treatment. Subsequently, this recommen-*

*dation was modified in the 2023 AHA/ACC CPG for the management of chronic CAD to IIa B.*

- In patients with MVD and LVEF  $\leq 35\%$ , CABG surgery is recommended to improve survival (COR I, LOE B). *This COR and LOE are in line with those of the 2021 ACC/AHA/SCAI Guideline for Coronary Artery Revascularization and 2023 AHA/ACC CPG for the management of chronic CAD.*
- In patients with functionally significant MVD and LVEF  $\leq 35\%$  who are at high surgical risk or not operable, PCI may be considered as an alternative to CABG surgery (COR IIb, LOE B). The evidence derived from the REVIVED-BCIS2 study has downgraded the recommendation for PCI in ischemic heart disease, representing a notable development. (13) *This scenario was defined as multifactorial (HT, anatomy, possibility of complete revascularization, diabetes and comorbidities) in the 2018 ESC CPG on revascularization with a COR IIa, LOE C. The 2021 AHA/ACC/SCI revascularization guideline recommended PCI only for patients with contraindication to cardiac surgery via the HT, without providing a COR. Finally, the 2023 AHA/ACC guidelines for the management of CAD stated that PCI is reasonable as an alternative to surgery to reduce events (COR IIa, LOE B).*

Based on the study by Perera et al., (13) the determination of viability did not obtain any recommendation in this section.

#### INOCA/ANOCA

This document features an extensive section dedicated to ischemia/angina with non-obstructive coronary arteries (INOCA/ANOCA), which is a notable shift from the 2019 CPG, where this topic was mentioned for the first time. The GPG include a solid algorithm for making the diagnosis, highlighting the role of angiography with coronary functional testing to define the endotype and to improve quality of life (COR I, LOE B). This is the current, widely accepted approach outlined by the leading CPG on the subject. (14) *The 2023 AHA/ACC CPG for the management of chronic CAD provided a lower COR (IIa) with the same LOE (B). Non-invasive functional testing has been downgraded to a COR IIb, LOE B.*

#### CONCLUSION

This long-awaited document requires a detailed reading due to its length, the quantity of information it contains, and the value of the changes it proposes. The workup process has evolved and the current role of ischemia, functional testing and CCTA merits a separate article. Medical treatment has incorporated significant advances, and the recommendations demonstrate its prognostic power compared to intervention. Coronary anatomy continues to be what ultimately defines revascularization and, finally, INOCA/ANOCA is positioned as a central issue in the diagnostic algorithm.

### Conflicts of interest

None declared.

(See authors' conflict of interests forms on the web/Additional material.)

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*Revista argentina de cardiología*  
vol. 92, no. 6, p. 444 - 447, 2024  
Sociedad Argentina de Cardiología,

**ISSN:** 0034-7000  
**ISSN-E:** 1850-3748

**DOI:** <https://doi.org/10.7775/rac.es.v92.i6.20835>