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SERVICES FOR SCIENCE AND EDUCATION

The 2024 ESC Guidelines for Chronic Coronary Syndromes: A Paradigm Shift in Risk Stratification and Therapeutic Strategies

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ABSTRACT

The 2024 European Society of Cardiology (ESC) guidelines on chronic coronary syndromes (CCS) introduce significant refinements in diagnosis, risk stratification, and therapeutic strategies, underscoring a shift toward precision medicine and personalized patient care. Moving beyond traditional phenotype classifications, CCS is now recognized as a spectrum, with risk assessment enhanced by coronary artery calcium scoring (CACS) and the risk factor-weighted clinical likelihood (RF-CL) model, improving predictive accuracy for adverse cardiovascular events. Therapeutic updates include optimized dual antiplatelet therapy (DAPT), clopidogrel monotherapy, and expanded use of P2Y12 inhibitors, aiming to balance ischemic protection with bleeding risks. The guidelines further reinforce the cardiovascular benefits of glucagon-like peptide-1 (GLP-1) receptor agonists and sodium–glucose cotransporter 2 (SGLT2) inhibitors beyond diabetes care. A comparison between ESC 2019 and ESC 2024 underscores a more individualized approach to CCS management, incorporating non-invasive imaging such as coronary computed tomography angiography (CCTA), cardiac magnetic resonance imaging (CMR), and positron emission tomography (PET)/single-photon emission computed tomography (SPECT) to refine diagnostic accuracy, while emphasizing the diamond model for medical therapy tailored to coronary pathophysiology and symptom severity. Additionally, the guidelines explore the role of anti-inflammatory therapies, particularly low-dose colchicine, in reducing cardiovascular events, reinforcing a paradigm shift toward integrated, risk-adapted strategies. These advancements signal a holistic transformation in CCS management, combining precision medicine, cutting-edge imaging tools, and emerging pharmacotherapies to enhance clinical decision-making and long-term patient outcomes, while future research should focus on refining antithrombotic regimens, assessing novel lipid-lowering agents, and evaluating anti-inflammatory strategies to ensure sustained improvements in cardiovascular care.

Keywords: Anti-inflammatory therapies, chronic coronary syndromes, coronary computed tomography angiography, dual antiplatelet therapy, ESC guidelines

INTRODUCTION

The 2024 European Society of Cardiology (ESC) guidelines on chronic coronary syndromes (CCS) [1] mark a significant departure from previous recommendations, notably the 2019 edition [2], as they embrace a more dynamic, individualized approach to patient care. While the

2019 guidelines categorized CCS into six distinct phenotypes [2], the latest iteration recognizes the condition as a continuum, influenced by atherosclerosis progression, metabolic dysfunction, and microvascular impairments [1]. This shift has led to refinements in risk stratification, most notably the integration of coronary artery calcium scoring and the risk factor-weighted clinical likelihood model, enhancing predictive accuracy for adverse cardiovascular events compared to earlier methods.

Beyond diagnostic enhancements, the ESC 2024 guidelines introduce key therapeutic innovations [1], building upon and, in some cases, modifying recommendations from 2019 [2]. The updated approach to dual antiplatelet therapy (DAPT) includes shortened protocols and increased reliance on clopidogrel monotherapy to optimize the balance between ischemic protection and bleeding risks. Additionally, the 2024 guidelines expand the role of glucagon-like peptide-1 (GLP-1) receptor agonists and sodium–glucose cotransporter 2 (SGLT2) inhibitors beyond diabetes management, emphasizing their cardiovascular protective effects—a notable evolution from their more limited application in the 2019 guidelines. Revascularization strategies have also evolved, shifting from anatomy-driven intervention decisions to a more nuanced strategy incorporating ischemic burden, comorbid conditions, and functional imaging parameters.

Advancements in imaging technologies reinforce the transformation seen between the 2019 and 2024 guidelines. The greater emphasis on non-invasive modalities, including coronary computed tomography angiography (CCTA), cardiac magnetic resonance (CMR) imaging, and positron emission tomography (PET)/single-photon emission computed tomography (SPECT), reflects a refined approach to CCS diagnostics, improving accuracy and clinical decision-making. Additionally, the increasing recognition of anti-inflammatory strategies, particularly low-dose colchicine, underscores the growing focus on inflammation as a contributing factor to cardiovascular risk, expanding upon discussions first introduced in the 2019 recommendations.

This commentary reflects on the paradigm shift introduced in the ESC 2024 guidelines [1], highlighting their evolution from the 2019 recommendations [1] and assessing their clinical implications. By transitioning toward risk-adapted and precision-driven strategies, CCS management now demands a multidimensional approach, integrating advanced imaging, emerging pharmacotherapies, and individualized treatment pathways. Future research must refine antithrombotic regimens, evaluate novel lipid-lowering agents, and assess anti-inflammatory interventions to ensure sustained improvements in CCS care. As cardiovascular medicine continues to evolve, understanding these updates will be crucial in navigating the changing landscape of CCS management.

RISK STRATIFICATION AND DIAGNOSTIC ADVANCEMENTS

Risk stratification is a critical component of CCS management, determining the likelihood of adverse cardiovascular events and guiding treatment strategies. The 2024 ESC guidelines introduce notable refinements, moving beyond traditional clinical scores to incorporate advanced imaging techniques and risk-prediction models for a more personalized assessment [1]. These updates enhance predictive accuracy, improving the ability to differentiate high-risk patients requiring intensive intervention from those who may benefit from conservative management.

Key Updates in Risk Stratification

The 2024 guidelines emphasize the use of coronary artery calcium scoring (CACS) and risk factor-weighted clinical likelihood (RF-CL) model to improve risk assessment. CACS, obtained via non-contrast cardiac CT, provides a direct measure of coronary atherosclerosis burden, aiding in refining cardiovascular risk beyond conventional assessments [1]. The RF-CL model integrates traditional risk factors, clinical symptoms, and imaging findings, allowing for a more dynamic and individualized approach to patient classification [1].

Additionally, the guidelines suggest expanding the role of CCTA for non-invasive anatomical assessment of coronary artery disease (CAD). CCTA has emerged as a frontline diagnostic tool, particularly for patients with low-to-intermediate risk, reducing the need for invasive coronary angiography when significant obstructive CAD is unlikely [1].

The integration of functional imaging modalities, such as PET, SPECT, and CMR, provides insights into myocardial viability and ischemia, guiding revascularization strategies (Table 1). Stress echocardiography remains a widely used option, but new data suggest that CMR offers superior characterization of scar tissue and myocardial perfusion abnormalities, influencing long-term treatment decisions [3].

Table 1: Comparison of Risk Stratification between ESC 2019 and ESC 2024 Guidelines

Aspect	ESC 2019 Guidelines	ESC 2024 Guidelines
Risk Stratification Approach	Predominantly based on clinical scores (e.g., SCORE, TIMI, GRACE)	Integrated CACS and RF-CL model for individualized assessment
Imaging Modalities	Stress echocardiography and invasive angiography prioritized	CCTA emphasized as a first-line non-invasive test
Myocardial Viability Assessment	PET/SPECT used selectively for revascularization decisions	CMR expanded for detailed viability and perfusion assessment
Personalized Risk Assessment	Limited individualized stratification based on standard scores	Dynamic risk stratification integrating clinical, imaging, and metabolic factors

Clinical Implications and Future Directions

The 2024 ESC guidelines shift risk assessment toward precision medicine, ensuring more accurate identification of high-risk patients while reducing unnecessary interventions [1]. However, questions remain about cost-effectiveness, accessibility, and standardization of advanced imaging, particularly in resource-limited settings. Future research should focus on further refining predictive models, exploring AI-driven risk stratification, and validating the long-term benefits of expanded imaging applications in CCS management.

ANTITHROMBOTIC THERAPY: REFINEMENTS IN BALANCING ISCHEMIC AND BLEEDING RISKS

Antithrombotic therapy remains a cornerstone of CCS management, aiming to prevent thrombotic events while minimizing bleeding complications [4]. The 2024 ESC guidelines introduce several refinements, emphasizing personalized approaches based on a patient's individual ischemic and bleeding risk profile. Significant updates include shorter DAPT durations, expanded use of clopidogrel monotherapy, and increased recognition of single antiplatelet therapy (SAPT) with P2Y12 inhibitors in select populations [1].

Key Updates in Antithrombotic Therapy

The ESC 2024 guidelines revise recommendations for DAPT duration in patients undergoing percutaneous coronary intervention (PCI), particularly those at high bleeding risk. While six months of DAPT remains the standard for most patients (Class I, Level A), emerging evidence supports early discontinuation (after 1–3 months) for low ischemic risk patients with high bleeding risk, transitioning to SAPT (Class I, Level A). This update stems from growing data indicating that shortened DAPT minimizes bleeding complications without significantly increasing thrombotic risks [1].

A major shift involves the equivalence of clopidogrel monotherapy (75 mg daily) to aspirin monotherapy (75–100 mg daily) for long-term management in patients with a history of myocardial infarction (MI) or PCI (Class I, Level A). Previously, clopidogrel was reserved for aspirin-intolerant patients or those with specific conditions (e.g., peripheral arterial disease or prior stroke), but new data suggest comparable efficacy in secondary prevention [5].

For patients with a history of coronary artery bypass grafting (CABG), aspirin monotherapy remains the standard treatment (Class I, Level A). Additionally, aspirin is now recommended for patients with significant obstructive CAD but no prior MI or revascularization (Class I, Level B) [1].

An additional update pertains to the duration of DAPT following PCI in patients without high bleeding or ischemic risk, where short DAPT (1–3 months) followed by SAPT may now be considered (Class IIb, Level B) [1]. Furthermore, SAPT with P2Y12 inhibitors (e.g., ticagrelor or clopidogrel) is increasingly recognized as a viable option for high-risk ischemic patients after the DAPT phase, providing effective ischemic protection while minimizing bleeding risks (Table 2).

Table 2: Comparison of Antithrombotic Therapy between ESC 2019 and ESC 2024 Guidelines

Aspect	ESC 2019 Guidelines	ESC 2024 Guidelines
DAPT Duration (PCI Patients)	Standard 6–12 months for most patients	Shortened 1–3 months DAPT for low ischemic, high bleeding risk patients
Clopidogrel vs. Aspirin Monotherapy	Clopidogrel reserved for aspirin-intolerant patients	Clopidogrel considered equally effective as aspirin for secondary prevention
SAPT for High-Risk Ischemic Patients	No strong recommendations for SAPT post-DAPT	SAPT with ticagrelor or clopidogrel increasingly recognized
Aspirin for Non-Revascularized CAD Patients	No explicit recommendation	Aspirin recommended for obstructive CAD without prior MI or PCI

Clinical Implications and Future Directions

These updates reflect a growing emphasis on individualized antithrombotic therapy, adapting DAPT duration and antiplatelet selection to specific patient profiles. However, uncertainties remain regarding the optimal long-term strategy, particularly for patients with borderline bleeding risk or complex CAD presentations. Future research should explore the role of

emerging oral anticoagulants, optimal SAPT choices for different CCS subgroups, and long-term comparative efficacy between aspirin and clopidogrel monotherapy [6].

LIPID-LOWERING THERAPIES: ADVANCES IN DYSLIPIDEMIA MANAGEMENT

Optimizing lipid levels remains a fundamental strategy in reducing cardiovascular risk for CCS patients. The 2024 ESC guidelines maintain stringent low-density lipoprotein cholesterol (LDL-C) targets, reaffirming ≤55 mg/dL for high-risk patients and ≤40 mg/dL for very high-risk patients. However, major advancements include the expanded role of bempedoic acid, increased focus on RNA interference (RNAi) therapies, and a reinforced recommendation for proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors, providing alternative pathways to LDL-C reduction beyond traditional statin therapy [1].

Key Updates in Lipid-Lowering Therapy

The most significant update involves the integration of bempedoic acid as a first-line non-statin option for statin-intolerant patients unable to reach LDL-C targets with ezetimibe alone (Class I, Level B). Bempedoic acid differs from statins by inhibiting cholesterol synthesis at an earlier step in the enzymatic chain, thereby avoiding muscular side effects linked to statins and improving tolerance in patients with statin-induced myopathy [7].

Additionally, the guidelines emphasize Inclisiran, a novel RNA interference (RNAi) therapy, which provides sustained LDL-C reduction with biannual dosing, offering benefits in long-term plaque stabilization and improved adherence. Inclisiran has demonstrated comparable efficacy to PCSK9 inhibitors, reinforcing its role as a practical alternative for patients requiring additional LDL-C lowering beyond statins and ezetimibe [8].

PCSK9 inhibitors, including alirocumab and evolocumab, remain strongly recommended for patients who fail to reach LDL-C targets on maximally tolerated statin therapy plus ezetimibe (Class I, Level A) [1]. Their subcutaneous administration ensures potent LDL-C reduction, particularly in high-risk populations, reinforcing their importance in aggressive lipid control strategies [9] (Table 3).

Table 3: Comparison of Lipid-Lowering Therapy between ESC 2019 and ESC 2024 Guidelines

Aspect	ESC 2019 Guidelines	ESC 2024 Guidelines
LDL-C Targets	≤55 mg/dL (high-risk), ≤40 mg/dL (very high-risk)	Unchanged from 2019 guidelines
Bempedoic Acid	No formal recommendation	Class I, Level B for statin-intolerant patients
PCSK9 Inhibitors	Recommended as adjunct therapy for high-risk patients	Reaffirmed as essential for patients failing statin + ezetimibe therapy
Inclisiran (RNAi Therapy)	Limited mention	Recognized as a practical alternative with biannual administration

Clinical Implications and Future Directions

The ESC 2024 guidelines reinforce aggressive LDL-C management, providing alternative therapeutic strategies for patients unable to tolerate statins or requiring intensified lipid lowering. However, cost, accessibility, and long-term adherence remain key barriers,

particularly for newer therapies like Inclisiran. Future research should explore head-to-head comparisons between PCSK9 inhibitors and RNAi therapies, evaluating long-term cardiovascular benefits and cost-effectiveness in real-world settings.

GLUCOSE-LOWERING THERAPIES IN CARDIOVASCULAR PROTECTION

Historically used in diabetes management, glucose-lowering drugs such as SGLT2 inhibitors and GLP-1 receptor agonists have demonstrated strong cardiovascular benefits, leading to their expanded role in CCS management [10]. The 2024 ESC guidelines formally integrate these therapies as primary interventions in patients with CCS, reinforcing their role in reducing cardiovascular events beyond their glucose-lowering effects. The guidelines establish clear recommendations for their use, based on evidence from major clinical trials, including EMPA-REG OUTCOME, CANVAS, DAPA-HF, and SELECT [11].

Key Updates in SGLT2 Inhibitors and GLP-1 Receptor Agonists

The ESC 2024 guidelines provide a Class I, Level A recommendation for the use of SGLT2 inhibitors and GLP-1 receptor agonists in patients with CCS and type 2 diabetes mellitus (T2DM), highlighting their ability to lower cardiovascular risk independently of glycated hemoglobin (HbA1c) levels [1]. Unlike traditional glucose-lowering agents, these drugs exert direct cardiovascular protective effects, including improved endothelial function, anti-inflammatory properties, and reduced oxidative stress, making them key components of CCS management [12].

A major update includes the recommendation of semaglutide, a GLP-1 receptor agonist, for use in non-diabetic patients with obesity (BMI >27 kg/m^2) based on findings from the SELECT trial [13], which demonstrated reduced cardiovascular mortality, myocardial infarction (MI), and stroke risk in overweight individuals (Class IIa, Level B). This marks a shift toward metabolic interventions in cardiovascular disease, reflecting the growing recognition of obesity as a central driver of atherosclerosis. Additionally, SGLT2 inhibitors, such as dapagliflozin and empagliflozin, have been emphasized for use in heart failure patients, particularly those with heart failure with preserved ejection fraction (HFpEF), reinforcing their role as disease-modifying therapies beyond CCS [1] (Table 4).

Table 4: Comparison of Glucose-Lowering Therapies between ESC 2019 and ESC 2024 Guidelines

Aspect	ESC 2019 Guidelines	ESC 2024 Guidelines
SGLT2 Inhibitors in CCS Patients	Limited recommendation outside diabetes care	Class I, Level A recommendation for CCS patients with T2DM
GLP-1 Receptor Agonists for Non-Diabetics	No formal endorsement	Class IIa, Level B recommendation for semaglutide in obese patients (BMI >27 kg/m^2)
SGLT2 Inhibitors in Heart Failure	Strongly recommended for heart failure with reduced ejection fraction (HFrEF)	Expanded indication for HFpEF, reinforcing cardiovascular benefits
Independent Cardiovascular Protection	Focus on HbA1c reduction	Recognized for direct anti-inflammatory and endothelial effects

Clinical Implications and Future Directions

These updates reinforce the cardiometabolic approach to CCS management, broadening the therapeutic landscape beyond conventional lipid-lowering and antithrombotic therapies [14]. However, questions remain regarding optimal drug selection, cost-effectiveness, and long-term data on non-diabetic populations. Future research should focus on combination strategies integrating GLP-1 receptor agonists, SGLT2 inhibitors, and lipid-modifying agents, assessing their synergistic effects on cardiovascular outcomes.

ANTI-INFLAMMATORY THERAPIES: THE EXPANDING ROLE OF INFLAMMATION IN CCS MANAGEMENT

Inflammation plays a critical role in the progression of atherosclerosis and CCS [15]. Recent evidence suggests that targeting residual inflammatory burden may provide additional cardiovascular protection, beyond conventional lipid-lowering and antithrombotic therapies [16]. The 2024 European Society of Cardiology (ESC) guidelines formally recognize anti-inflammatory therapy as a viable adjunctive treatment, particularly for patients with elevated inflammatory markers or high residual risk despite optimized medical therapy. Notable advancements include the incorporation of low-dose colchicine, reassessment of canakinumab, and exploration of novel inflammation-modulating agents [1].

Key Updates in Anti-Inflammatory Therapy

The most pivotal update is the recommendation of low-dose colchicine (0.5 mg daily) in patients with atherosclerotic CAD to reduce myocardial infarction (MI), stroke, and the need for revascularization (Class IIa, Level A) [1]. Evidence from the COLCOT and LODOCO2 trials demonstrated significant reductions in major adverse cardiovascular events (MACE) in both post-MI and stable CCS populations, reinforcing the utility of colchicine as a secondary prevention strategy [17].

In contrast, canakinumab, an interleukin-1β (IL-1β) inhibitor, which previously showed promise in reducing cardiovascular events in the CANTOS trial [18], has not been recommended due to cost concerns and the absence of long-term efficacy data in broader CCS populations (Table 5). However, ongoing trials continue to explore alternative inflammation-modulating agents, including methotrexate and novel cytokine inhibitors, potentially offering new avenues for targeted vascular inflammation reduction [19].

Table 5: Comparison of Anti-Inflammatory Therapy between ESC 2019 and ESC 2024 Guidelines

Aspect	ESC 2019 Guidelines	ESC 2024 Guidelines
Colchicine for Cardiovascular Prevention	Limited recognition outside pericarditis treatment	Class IIa, Level A for CCS patients with atherosclerotic CAD
Canakinumab (IL-1β Inhibitor)	Promising data but not widely endorsed	Not recommended due to cost-effectiveness concerns
Future Anti-Inflammatory Approaches	Focus on lifestyle and statins	Increasing exploration of novel inflammation-targeted therapies

Clinical Implications and Future Directions

These updates reflect the growing acknowledgment of inflammation as a key driver of cardiovascular risk [20]. The ESC 2024 guidelines reinforce colchicine as a viable adjunct, but

further research is needed to determine long-term safety, optimal patient selection, and efficacy of newer anti-inflammatory agents. Future investigations should focus on integrating precision biomarkers, such as C-reactive protein (CRP) and interleukin-6 (IL-6), to better tailor anti-inflammatory treatment strategies in CCS populations [21].

REVASCULARIZATION STRATEGIES: REFINING DECISION-MAKING IN CCS

Revascularization remains a key intervention in CCS management, offering improved symptom relief and cardiovascular outcomes for select patient groups. The 2024 ESC guidelines build upon prior recommendations by refining patient selection criteria, integrating functional imaging assessments, and emphasizing shared decision-making approaches. A more individualized strategy now guides the choice between PCI and CABG based on ischemic burden, anatomical complexity, and comorbid conditions [1].

Key Updates in Revascularization Strategies

A major shift in the 2024 guidelines involves prioritizing functional ischemia assessments before proceeding with invasive interventions [1]. While the 2019 guidelines relied heavily on angiographic severity [2], the latest recommendations emphasize fractional flow reserve (FFR) and stress imaging modalities to confirm clinical relevance of stenosis before selecting revascularization options [1].

Additionally, the ESC 2024 guidelines reinforce CABG as the preferred approach for multivessel disease with diabetes (Class I, Level A), highlighting superior long-term cardiovascular benefits in this population compared to PCI [1]. Conversely, PCI remains strongly recommended for single-vessel disease affecting major epicardial arteries, provided that FFR or stress imaging confirms significant functional ischemia (Class I, Level A) [1].

Another key update pertains to chronic total occlusion (CTO) management, where PCI is now considered reasonable (Class IIa, Level B) for patients with persistent symptoms despite optimal medical therapy, provided that procedural success rates are high and risk-benefit ratios favor intervention [1] (Table 6).

Table 6: Comparison of Revascularization Strategies between ESC 2019 and ESC 2024 Guidelines

Aspect	ESC 2019 Guidelines	ESC 2024 Guidelines
Revascularization Criteria	Based primarily on angiographic severity	Emphasis on functional ischemia assessment via FFR and imaging
CABG vs. PCI in Diabetes	CABG preferred for multivessel disease	Reaffirmed with stronger evidence (Class I, Level A)
Chronic Total Occlusion (CTO) PCI	Limited recommendations	PCI now considered reasonable for symptom relief (Class IIa, Level B)
Shared Decision-Making	Encouraged but not explicitly defined	Strengthened emphasis on patient preference, quality of life, and risk-benefit assessment

Clinical Implications and Future Directions

These refinements underscore the importance of functional ischemia assessment, ensuring that revascularization decisions are evidence-driven rather than relying solely on angiographic

findings [22]. However, the role of emerging technologies, such as artificial intelligence (AI)-driven imaging interpretation, remains unclear. Future studies should explore how advanced algorithms can optimize revascularization strategies, further improving long-term patient outcomes.

MANAGEMENT OF PATIENTS WITH SEVERELY DEPRESSED EJECTION FRACTION: OPTIMIZING HEART FAILURE STRATEGIES

Patients with severely depressed left ventricular ejection fraction (LVEF ≤35%) represent a high-risk subgroup within CCS management, requiring individualized treatment strategies to improve survival and quality of life [23]. The 2024 ESC guidelines introduce refinements in pharmacological therapy, device-based interventions, and advanced heart failure care, reinforcing multidisciplinary approaches to optimize patient outcomes. Key updates include expanding the use of SGLT2 inhibitors, strengthening indications for implantable cardioverter-defibrillators (ICDs) and cardiac resynchronization therapy (CRT), and integrating heart failure phenotyping to guide therapy selection more effectively [1].

Key Updates in Management of Severely Depressed Ejection Fraction

A major update in the 2024 guidelines is the stronger recommendation for SGLT2 inhibitors (dapagliflozin and empagliflozin) in heart failure with reduced ejection fraction (HFrEF), emphasizing their cardioprotective effects beyond glucose control (Class I, Level A) [1]. These agents reduce hospitalizations, improve left ventricular remodeling, and enhance symptom management, reinforcing their role alongside angiotensin-converting enzyme (ACE) inhibitors, beta-blockers, and mineralocorticoid receptor antagonists (MRAs).

Additionally, the guidelines reaffirm ICD and CRT indications, advocating for early device implantation in high-risk patients (Class I, Level A) [1]. ICD therapy remains strongly recommended for primary prevention in patients with symptomatic heart failure (New York Heart Association [NYHA] II-III) and LVEF ≤35%, while CRT is recommended for patients with LVEF ≤35% and left bundle branch block (LBBB) ≥150 ms, given its proven benefits in reducing morbidity and mortality [24]. Another critical refinement is the greater emphasis on heart failure phenotyping, recognizing distinct CCS subtypes and tailoring pharmacological interventions accordingly. For patients with advanced heart failure, the guidelines reinforce early referral to specialized heart failure centers, supporting timely evaluation for left ventricular assist devices (LVADs) or heart transplantation in refractory cases [1] (Table 7).

Table 7: Comparison of Heart Failure Strategies between ESC 2019 and ESC 2024 Guidelines

Aspect	ESC 2019 Guidelines	ESC 2024 Guidelines
Pharmacological Therapy	Standard therapy with ACE inhibitors, beta-blockers, and MRAs	Expanded role for SGLT2 inhibitors in HFrEF (Class I, Level A)
Device Therapy (ICD/CRT)	ICD recommended for EF ≤35% with NYHA II-III	Reinforced early ICD/CRT implantation in high-risk patients
Heart Failure Phenotyping	Limited focus on personalized approaches	Greater emphasis on phenotyping to guide therapy selection
Advanced Heart Failure Care	Referral for heart transplant or LVAD in refractory cases	Strengthened recommendations for early referral to specialized centers

Clinical Implications and Future Directions

These refinements underscore the importance of early intervention, optimized pharmacological strategies, and improved device therapy utilization in patients with severely depressed ejection fraction. However, questions remain regarding long-term heart failure phenotyping, optimal sequencing of novel pharmacological agents, and the role of AI in predicting disease progression. Future studies should focus on precision heart failure biomarkers, AI-driven decision support models, and expanding access to advanced heart failure therapies to further refine CCS management for this high-risk group.

EMERGING THERAPEUTIC APPROACHES AND FUTURE DIRECTIONS

The 2024 ESC guidelines recognize the evolving nature of CCS management, integrating novel pharmacological, procedural, and preventative strategies to enhance patient outcomes. While existing therapies focus on lipid-lowering, antithrombotic strategies, and revascularization, new avenues in metabolic modulation, microvascular disease targeting, and AI-driven diagnostics are gaining momentum [25]. These innovations reflect a growing emphasis on individualized treatment approaches, improving risk stratification, optimizing therapy selection, and ensuring long-term cardiovascular protection.

Key Emerging Therapeutic Strategies

A central area of focus involves metabolic modulation, with trials exploring the impact of SGLT1 inhibitors and dual incretin receptor agonists on cardiovascular outcomes [26, 27]. These agents target energy metabolism, endothelial function, and vascular inflammation, showing promise in reducing myocardial stress and improving long-term plaque stability.

Additionally, microvascular dysfunction is increasingly recognized as a major contributor to CCS symptoms, particularly in angina with no obstructive coronary artery disease (ANOCA) and ischemia with no obstructive coronary artery disease (INOCA) [28]. Novel therapies, such as ranolazine and ivabradine, aim to target microvascular impairment, improving symptom relief and myocardial perfusion [29, 30].

AI is gaining traction in predictive analytics and diagnostic accuracy, particularly in refining risk stratification models and optimizing imaging interpretation [31, 32]. AI-driven algorithms are being tested in CCTA, CMR, and FFR analysis, allowing for earlier detection of high-risk patients and more precise intervention planning [33].

The guidelines also highlight gene therapy as a potential future frontier, with ongoing studies examining the role of vascular endothelial growth factor (VEGF) modulation and stem cell therapy in atherosclerosis regression and myocardial repair (Table 8).

Table 8: Comparison of Emerging Therapeutic Approaches between ESC 2019 and ESC 2024 Guidelines

Aspect	ESC 2019 Guidelines	ESC 2024 Guidelines
Metabolic Modulation	Focused on glucose-lowering effects in diabetics	Expanded role for cardiovascular benefits beyond diabetes
Microvascular Disease	Limited guidance on ANOCA/INOCA patients	Recognition of targeted therapies for microvascular dysfunction

AI in Risk Stratification	No formal recommendations	Increasing focus on AI-driven predictive analytics
Gene Therapy & Regenerative Medicine	Considered experimental	Growing interest in VEGF modulation and stem cell applications

Clinical Implications and Future Research Priorities

These updates signal a shift toward a more dynamic, integrative approach in CCS management, incorporating advanced therapeutic strategies beyond conventional pharmacological and procedural interventions. Future research should focus on long-term efficacy of metabolic modulators, validation of AI-driven diagnostics in clinical practice, and development of effective gene therapies for cardiov Conclusion

CONCLUSION

The 2024 ESC guidelines mark a significant evolution in CCS management, shifting towards precision medicine, individualized risk assessment, and multimodal therapeutic strategies. These updates emphasize functional imaging in risk stratification, recognizing the importance of non-invasive tools such as CCTA and CMR. Additionally, refinements in antithrombotic therapy, including shortened DAPT protocols and expanded use of clopidogrel monotherapy, provide a more tailored approach to balancing ischemic and bleeding risks. ascular disease reversal.

Pharmacological advancements introduce SGLT2 inhibitors and GLP-1 receptor agonists as integral components of CCS management, reinforcing their cardiovascular protective effects beyond glucose control. Furthermore, the growing role of anti-inflammatory therapy, particularly low-dose colchicine, reflects a paradigm shift towards targeting residual inflammatory risk to improve cardiovascular outcomes.

The guidelines also refine revascularization strategies, emphasizing shared decision-making, functional ischemia assessment, and individualized procedural selection. The recognition of microvascular dysfunction and metabolic modulation as emerging therapeutic areas highlights the expanding scope of CCS management, paving the way for future innovations in regenerative medicine, AI-driven diagnostics, and gene therapy.

However, critical questions remain regarding cost-effectiveness, accessibility, and real-world implementation of newer therapies. Future research should focus on optimizing therapeutic combinations, validating AI-driven risk models, and refining precision biomarkers to ensure sustained progress in CCS treatment. These refinements collectively enhance patient-centered care, reinforcing the importance of integrating novel pharmacological, procedural, and preventative strategies to improve long-term cardiovascular outcomes.

Author Contribution

The author solely conceived, designed, wrote, revised, and approved the final manuscript for publication.

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References

1. Vrints C, Andreotti F, Koskinas KC, Rossello X, Adamo M, Ainslie J, Banning AP, Budaj A, Buechel RR, Chiariello GA, Chieffo A, Christodorescu RM, Deaton C, Doenst T, Jones HW, Kunadian V, Mehilli J, Milojevic M, Piek JJ, Pugliese F, Rubboli A, Semb AG, Senior R, Ten Berg JM, Van Belle E, Van Craenenbroeck EM, Vidal-Perez R, Winther S; ESC Scientific Document Group. 2024 ESC Guidelines for the management of chronic coronary syndromes. Eur Heart J. 2024; 45:3415-3537. doi: 10.1093/eurheartj/ehae177. Erratum in: Eur Heart J. 2025 Feb 21: ehaf079. doi: 10.1093/eurheartj/ehaf079.

2. Knuuti J, Wijns W, Saraste A, Capodanno D, Barbato E, Funck-Brentano C, Prescott E, Storey RF, Deaton C, Cuisset T, Agewall S, Dickstein K, Edvardsen T, Escaned J, Gersh BJ, Svitil P, Gilard M, Hasdai D, Hatala R, Mahfoud F, Masip J, Muneretto C, Valgimigli M, Achenbach S, Bax JJ; ESC Scientific Document Group. 2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes. Eur Heart J. 2020; 41:407-477. doi: 10.1093/eurheartj/ehz425. Erratum in: Eur Heart J. 2020; 41:4242. doi: 10.1093/eurheartj/ehz825.

3. Hamilton-Craig C, Ugander M, Greenwood JP, Kozor R. Stress perfusion cardiovascular magnetic resonance imaging: a guide for the general cardiologist. Heart. 2023; 109:428-433. doi: 10.1136/heartjnl-2022-321630.

4. Crea F. Thrombotic and bleeding complications during antithrombotic treatment: the need for new therapeutic targets. Eur Heart J. 2023; 44:1767-1770. doi: 10.1093/eurheartj/ehad285.

5. Wang Z, Zhu S, Zhu J, Jiang Z, Ren Y. Comparison of P2Y12 inhibitors and aspirin in secondary prevention of coronary events: a meta-analysis of RCTs. BMC Cardiovasc Disord. 2025; 25:207. doi: 10.1186/s12872-025-04668-x.

6. Storey RF. Individualising Antithrombotic Strategies for Acute and Chronic Coronary Syndromes. Interv Cardiol. 2024;19: e07. doi: 10.15420/icr.2023.44.

7. Ray KK, Bays HE, Catapano AL, Lalwani ND, Bloedon LT, Sterling LR, Robinson PL, Ballantyne CM; CLEAR Harmony Trial. Safety and Efficacy of Bempedoic Acid to Reduce LDL Cholesterol. N Engl J Med. 2019; 380:1022-1032. doi: 10.1056/NEJMoa1803917.

8. Mansoor T, Rao BH, Gupta K, Parikh SS, Abramov D, Mehta A, Al Rifai M, Virani SS, Nambi V, Minhas AMK, Koshy SKG. Inclisiran as a siRNA Inhibitor of Proprotein Convertase Subtilisin/Kexin Type 9 (PCSK9); Past, Present, and Future. Am J Cardiovasc Drugs. 2024 Dec 20. doi: 10.1007/s40256-024-00712-x. Epub ahead of print.

9. Garwood CL, Cabral KP, Brown R, Dixon DL. Current and emerging PCSK9-directed therapies to reduce LDL-C and ASCVD risk: A state-of-the-art review. Pharmacotherapy. 2025; 45:54-65. doi: 10.1002/phar.4635.

10. Simms-Williams N, Treves N, Yin H, Lu S, Yu O, Pradhan R, Renoux C, Suissa S, Azoulay L. Effect of combination treatment with glucagon-like peptide-1 receptor agonists and sodium-glucose cotransporter-2 inhibitors on incidence of cardiovascular and serious renal events: population-based cohort study. BMJ. 2024;385: e078242. doi: 10.1136/bmj-2023-078242. Erratum in: BMJ. 2024;385: q1094. doi: 10.1136/bmj. q1094. Erratum in: BMJ. 2024 Jun 5;385: q1237. doi: 10.1136/bmj. q1237.

11. Rosano G, Quek D, Martínez F. Sodium-Glucose Co-transporter 2 Inhibitors in Heart Failure: Recent Data and Implications for Practice. Card Fail Rev. 2020;6: e31. doi: 10.15420/cfr.2020.23.

12. Cersosimo A, Salerno N, Sabatino J, Scatteia A, Bisaccia G, De Rosa S, Dellegrottaglie S, Bucciarelli-Ducci C, Torella D, Leo I. Underlying mechanisms and cardioprotective effects of SGLT2i and GLP-1Ra: insights from cardiovascular magnetic resonance. Cardiovasc Diabetol. 2024; 23:94. doi: 10.1186/s12933-024-02181-7.

13. Kushner RF, Ryan DH, Deanfield J, Kokkinos A, Cercato C, Wilding J, Burguera B, Wu CC, Craciun AE, Pall D, Hramiak I, Hjelmesæth J, Harder-Lauridsen NM, Weimers P, Jeppesen OK, Kallenbach K, Lincoff AM, Lingvay I. Safety profile of semaglutide versus placebo in the SELECT study: a randomized controlled trial. Obesity (Silver Spring). 2025; 33:452-462. doi: 10.1002/oby.24222.

14. Sebastian SA, Padda I, Johal G. Cardiovascular-Kidney-Metabolic (CKM) syndrome: A state-of-the-art review. Curr Probl Cardiol. 2024; 49:102344. doi: 10.1016/j.cpcardiol.2023.102344.

15. Libby P. Inflammation during the life cycle of the atherosclerotic plaque. Cardiovasc Res. 2021 Nov 22;117(13):2525-2536. doi: 10.1093/cvr/cvab303.

16. Ajala ON, Everett BM. Targeting Inflammation to Reduce Residual Cardiovascular Risk. Curr Atheroscler Rep. 2020; 22:66. doi: 10.1007/s11883-020-00883-3.

17. Bonaventura A, Potere N, Liberale L, Kraler S, Weber BN, Abbate A. Colchicine in Coronary Artery Disease: Where Do We Stand? J Cardiovasc Pharmacol. 2025; 85:243-247. doi: 10.1097/FJC.0000000000001672.

18. Svensson EC, Madar A, Campbell CD, He Y, Sultan M, Healey ML, Xu H, D'Aco K, Fernandez A, Wache-Mainier C, Libby P, Ridker PM, Beste MT, Basson CT. TET2-Driven Clonal Hematopoiesis and Response to Canakinumab: An Exploratory Analysis of the CANTOS Randomized Clinical Trial. JAMA Cardiol. 2022; 7:521-528. doi: 10.1001/jamacardio.2022.0386.

19. Ait-Oufella H, Libby P. Inflammation and Atherosclerosis: Prospects for Clinical Trials. Arterioscler Thromb Vasc Biol. 2024; 44:1899-1905. doi: 10.1161/ATVBAHA.124.320155.

20. Agnello F, Capodanno D. Anti-inflammatory strategies for atherosclerotic artery disease. Expert Opin Drug Saf. 2022; 21:661-672. doi: 10.1080/14740338.2022.2036717.

21. Held C, White HD, Stewart RAH, Budaj A, Cannon CP, Hochman JS, Koenig W, Siegbahn A, Steg PG, Soffer J, Weaver WD, Östlund O, Wallentin L; STABILITY Investigators. Inflammatory Biomarkers Interleukin-6 and C-Reactive Protein and Outcomes in Stable Coronary Heart Disease: Experiences from the STABILITY (Stabilization of Atherosclerotic Plaque by Initiation of Darapladib Therapy) Trial. J Am Heart Assoc. 2017;6: e005077. doi: 10.1161/JAHA.116.005077.

22. Prati F, Albertucci M, Biccire' FG, Gatto L. The role of functional assessment in the management of ischaemic heart disease. Eur Heart J Suppl. 2025;27(Suppl 1): i27-i30. doi: 10.1093/eurheartjsupp/suae121.

23. Moreno-Angarita A, Peña D, de León JDL, Estacio M, Vila LP, Muñoz MI, Cadavid-Alvear E. Current indications and surgical strategies for myocardial revascularization in patients with left ventricular dysfunction: a scoping review. J Cardiothorac Surg. 2024; 19:469. doi: 10.1186/s13019-024-02844-2.

24. Yehya A, Lopez J, Sauer AJ, Davis JD, Ibrahim NE, Tung R, Bozkurt B, Fonarow GC, Al-Khatib SM. Revisiting ICD Therapy for Primary Prevention in Patients with Heart Failure and Reduced Ejection Fraction. JACC Heart Fail. 2025; 13:1-13. doi: 10.1016/j.jchf.2024.09.014.

25. Choi AD, Marques H, Kumar V, Griffin WF, Rahban H, Karlsberg RP, Zeman RK, Katz RJ, Earls JP. CT Evaluation by Artificial Intelligence for Atherosclerosis, Stenosis and Vascular Morphology (CLARIFY): A Multi-center, international study. J Cardiovasc Comput Tomogr. 2021; 15:470-476. doi: 10.1016/j.jcct.2021.05.004.

26. Lin ZM, Gao HY, Shi SH, Li YT. Mizagliflozin ameliorates diabetes induced kidney injury by inhibitor inhibit inflammation and oxidative stress. World J Diabetes. 2025; 16:92711. doi: 10.4239/wjd. v16.i1.92711.

27. Bailey CJ, Flatt PR, Conlon JM. Multifunctional incretin peptides in therapies for type 2 diabetes, obesity and associated co-morbidities. Peptides. 2025; 187:171380. doi: 10.1016/j.peptides.2025.171380.

28. Webb CM, George M, Collins P. The 2024 European Society of Cardiology guidelines for chronic coronary syndromes: good news for angina and non-obstructive coronary artery (ANOCA)/ischaemia and non-obstructive coronary artery (INOCA) patients? Eur Heart J Open. 2025;5: oeaf016. doi: 10.1093/ehjopen/oeaf016.

29. Sharp RP, Patatanian E, Sirajuddin R. Use of Ranolazine for the Treatment of Coronary Microvascular Dysfunction. Am J Cardiovasc Drugs. 2021; 21:513-521. doi: 10.1007/s40256-020-00462-6.

30. Cacciapuoti F. Ranolazine and Ivabradine: two different modalities to act against ischemic heart disease. Ther Adv Cardiovasc Dis. 2016; 10:98-102. doi: 10.1177/1753944716636042.

31. Awasthi S, Sachdeva N, Gupta Y, Anto AG, Asfahan S, Abbou R, Bade S, Sood S, Hegstrom L, Vellanki N, Alger HM, Babu M, Medina-Inojosa JR, McCully RB, Lerman A, Stampehl M, Barve R, Attia ZI, Friedman PA, Soundararajan V, Lopez-Jimenez F. Identification and risk stratification of coronary disease by artificial intelligence-enabled ECG. EClinicalMedicine. 2023; 65:102259. doi: 10.1016/j.eclinm.2023.102259.

32. Zhang Y, Feng Y, Sun J, Zhang L, Ding Z, Wang L, Zhao K, Pan Z, Li Q, Guo N, Xie X. Fully automated artificial intelligence-based coronary CT angiography image processing: efficiency, diagnostic capability, and risk stratification. Eur Radiol. 2024; 34:4909-4919. doi: 10.1007/s00330-023-10494-6.

33. Guo B, Jiang M, Guo X, Tang C, Zhong J, Lu M, Liu C, Zhang X, Qiao H, Zhou F, Xu P, Xue Y, Zheng M, Hou Y, Wang Y, Zhang J, Zhang B, Zhang D, Xu L, Hu X, Zhou C, Li J, Yang Z, Mao X, Lu G, Zhang L. Diagnostic and prognostic performance of artificial intelligence-based fully-automated on-site CT-FFR in patients with CAD. Sci Bull (Beijing). 2024; 69:1472-1485. doi: 10.1016/j.scib.2024.03.053.