2019 ESC GUIDELINES ON CHRONIC CORONARY SYNDROMES: ONE STEP FORWARD, TWO STEPS BACK

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For decades, it was assumed that a close link existed between coronary atherosclerotic obstructions and myocardial ischemia.[1] However, a large body of evidence has strongly challenged this assumption, suggesting that myocardial ischemia has a multifactorial nature where coronary artery obstructions are only one factor in the development of ischemic heart disease.[2] The 2013 ESC guidelines[3] partially acknowledged that multiple mechanisms may precipitate myocardial ischemia, warning that these mechanisms are not mutually exclusive and that they may change in time within the same patient. Consequently, these guidelines strongly downgraded the diagnostic role of both invasive and noninvasive coronary angiography.

The 2019 ESC guidelines[4] included the word "syndrome" in the title, which refers to a cluster of symptoms that may be associated with multiple mechanisms. Unfortunately, these guidelines do not appear consistent with their initial definition.

GUIDELINE INCONSISTENCIES

Lack of a diagnostic pathway and distinct therapeutic approach

No specific diagnostic pathway is presented to identify the mechanism(s) responsible for myocardial ischemia in individual patients and, after identifying the responsible mechanism(s), no distinct therapeutic approach is suggested. In addition, throughout the guidelines, no clear distinction is made between the diagnosis of myocardial ischemia and the identification of the responsible mechanism(s). Clinically detectable manifestations of myocardial ischemia include typical angina, typical ECG changes, regional wall dysfunction at echocardiography, perfusion defect at myocardial scan, and transcoronary lactate extraction at invasive assessment. The presence or absence of coronary atherosclerotic obstructions can no longer be considered as a surrogate for myocardial ischemia, as suggested by the high prevalence of absent or minor coronary artery disease in patients with proven myocardial ischemia (FAME 2[5] and CorMicA[6]).

The diagnostic algorithms are stubbornly focused on the identification of atherosclerotic obstructions and/or the estimation of their probability. Even after a marked reduction in the so-called pretest probability in both men and women, these guidelines fail to realize that, compared with men, women have about half the prevalence of coronary atherosclerosis, but a similar level of severe myocardial ischemia, with an even worse prognosis.

Considering angina and chest pain equivalent

In the guidelines, angina and chest pain are considered equivalent. Furthermore, the addition of dyspnea, without objective evidence of ischemia, all contribute to an unjustified enlargement of the "patient population," predisposing patients to an unjustified increase in investigations and procedures. Currently, 25.7% of patients undergoing percutaneous coronary intervention for stable coronary artery disease have no symptoms, and, moreover, many patients have minimal symptoms.[7] The recent trend in trials and registries to consider "chest pain" as an inclusion criteria instead of "angina" (only 22% of patients in the SCOT-HEART trial[8] had symptoms suggestive of real angina and only 5% in the CLARIFY registry[9] had angina and proven ischemia) dilutes the events, limits the chance to prove the efficacy of any treatment, and makes it difficult to appreciate the real prognostic impact of angina/ischemia. In practice, it makes it impossible to understand to whom the conclusions apply, ie, to the general population or to the patients with real angina.

Clinical scenarios based on coronary artery disease with or without confirmation of myocardial ischemia

An arbitrary and wide-ranging list of clinical scenarios was proposed, including (i) patients with suspected coronary artery disease and "stable" angina symptoms and/or dyspnea; (ii) patients with new-onset heart failure or left ventricular dysfunction and suspected coronary artery disease; (iii) asymptomatic and symptomatic patients with stabilized symptoms <1 year after an acute coronary syndrome or patients with a recent revascularization; (iv) asymptomatic and symptomatic patients >1 year after initial diagnosis or revascularization; (v) patients with angina and suspected vasospastic or microvascular disease; and (vi) asymptomatic subjects in whom coronary artery disease is detected at screening. Each case is again based on the presence of coronary artery disease, independently from the presence or absence of symptoms or proven/unproven myocardial ischemia, taking it to the point that the simple fact of having undergone a revascularization procedure makes the patient ischemic for life. The authors do not consider that a large fraction of revascularizations are performed in the absence of angina, in the absence of proven ischemia, and in patients who are under no medical therapy.[10-12]

Screening for coronary artery disease in asymptomatic patients

An entire section is dedicated to the screening of coronary artery disease in asymptomatic patients, which could be justified in an asymptomatic patient with proven myocardial ischemia. Otherwise, given the much larger prevalence of coronary atherosclerosis as compared with myocardial ischemia (10 to 1 in pathology reports), this recommendation may result in an incredible number of false-positive patients (no ischemia–coronary atherosclerosis) undergoing investigations and procedures. This approach looks even less understandable given the lack of any prognostic benefit of elective revascularization procedures and the growing awareness of the adverse effect of percutaneous coronary interventions (12.5% of periprocedural myocardial infarction,[13] a concerning rate of intraprocedural cardiac arrest and death,[14] a high rate of early unplanned hospital readmissions,[15] and 30% to 40% recurrence or persistence of angina.[16]

Therapeutic recommendations appear largely unsupported by conclusive evidence

The shift from a "first-to-second line" approach to a "step-wise" approach does not address the need for selecting a drug based on the pathogenesis of ischemia. This algorithm is even more surprising because the manuscript acknowledges the absence of any evidence of the superiority of one drug versus another, and it does not consider adverse effects and patients' tolerability in a life-long treatment.

The indication for β-blockers or calcium channel blockers as a "first-line" treatment is based on a paper[17] that concludes by saying that "beta blockers are no more effective than other anti-anginal agents on prophylaxis of myocardial ischemia in stable angina patients" and on a paper dating back more than 20 years.[18] Even more surprising is the maintenance of β-blockers as a first-step option, alternatively to calcium channel blockers, after the acknowledgement of coronary vasospasm as a possible pathogenetic mechanism of angina.

The upgrade of long-acting nitrates, recommended even before ivabradine, ranolazine, trimetazidine and nicorandil, does not appear to be supported by scientific evidence, as one of the meta-analyses,[19] on which it is based, reports that "too few trials compared nitrates with calcium antagonists or β-blockers to draw firm conclusions about relative efficacy," and the second meta-analysis[20] is based on studies with very small patient numbers, with open-label designs, and with almost no other background therapy that are comparing long-acting nitrates with placebo, showing nonconclusive results (nonsignificant *P* values) on the efficacy of long-acting nitrates vs placebo after 24 hours. Additionally, the new guidelines did not consider the recent reports suggesting an increase in major adverse cardiac events with the long-term use of these agents.[21,22]

Even more surprising is the recommendation to combine ivabradine with nondihydropyridine calcium channel blockers, which has been shown to be detrimental and therefore clearly contraindicated.

Similarly, the recommendation to consider revascularization in asymptomatic patients with no proven ischemia is not based on evidence, given that 61 randomized controlled trials and 15 meta-analyses have failed to prove any prognostic benefits of elective revascularization versus optimal medical therapy. ■

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