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Editorial

Comments on the 2015 ESC Guidelines for the Management of Acute Coronary Syndromes in Patients Presenting Without Persistent ST-segment Elevation

Comentarios a la guía ESC 2015 sobre el tratamiento de los síndromes coronarios agudos en pacientes sin elevación persistente del segmento ST

SEC Working Group for the 2015 ESC Guidelines for the Management of Acute Coronary Syndromes in Patients Presenting Without Persistent ST-segment Elevation, Expert Reviewers for the 2015 ESC Guidelines for the Management of Acute Coronary Syndromes in Patients Presenting Without Persistent ST-segment Elevation and the SEC Guidelines Committee[◊]

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INTRODUCTION

The guidelines of the European Society of Cardiology (ESC) are endorsed by the Spanish Society of Cardiology (SEC). Since 2011, the publication of the translation of the guidelines in *Revista Española de Cardiología* has been accompanied by a critical review article that is written by a group of authors coordinated by the SEC Guidelines Committee.[1]

This article discusses the 2015 ESC guidelines for the management of non–ST-segment elevation acute coronary syndromes (NSTEACS).[2] The Guidelines Committee designated a working group composed of members nominated by the SEC and the Spanish Society of Thoracic and Cardiovascular Surgery. The document was divided into parts that were sent to the members of the working group and, based on their comments, a manuscript was written and reevaluated by the group and by reviewers proposed by the SEC Working Group on Ischemic Heart Disease and Acute Cardiovascular Care.

GENERAL COMMENTS ON THE METHODOLOGY

The recommendations of the guidelines are summarized in tables that include: *a)* the class of recommendation, depending on whether there is evidence or agreement that a treatment or procedure is indicated (class I), should be considered (class IIa), may be considered (class IIb) or is not recommended (class III); *b)* the level of evidence, which can consist of multiple clinical trials or meta-analyses (level of evidence A), a single trial or large nonrandomized studies (level of evidence B), or expert consensus or small studies (level of evidence C); and *c)* literature references. Sixteen Tables are presented with 134 recommendations, less than two thirds of which are categorical (79 in class I, 8 in class III) and 40% are supported by level of evidence C, showing that there remain areas of uncertainty in the management of these patients.

One new feature is the inclusion of extensive supplementary material in an online Appendix, as well as a series of questions and responses taken from case reports, which will be useful to clarify concepts that appear in the guidelines.

SUMMARY OF THE MAJOR SECTIONS OF THE GUIDELINES

In the present article, Table 1 summarizes the most relevant or novel aspects and Table 2, the most debatable aspects, according to the working group.

Definitions and Diagnosis

The guidelines adopt the universal definition of acute myocardial infarction (AMI). For troponin measurement, high-sensitivity methods are recommended over conventional approaches because of their higher negative predictive value for AMI and because they facilitate an earlier diagnosis. Of the remaining biomarkers, the guidelines mention only creatine kinase MB fraction, which can aid in estimating the timing of myocardial injury and detect early reinfarction, and copeptin, a marker of endogenous stress that may have added value in enabling the early rule-out of AMI.

Although high-sensitivity troponin is the biomarker of choice, it has limitations. Slight elevations have a moderate positive predictive value for AMI and may be due to other causes. Moreover, although the rising and falling pattern in biomarker levels (delta) could allow differentiation between acute and chronic injury, the guidelines do not specify the significant delta values. These values differ widely from one study to another and may vary according to the reagents used,[3] although the guidelines mention that the higher these values, the greater the probability of AMI.

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◊The names of all the authors of the article are listed in the Appendix.

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Table 1
The Most Novel or Relevant Aspects of the 2015 ESC Guidelines for Non–ST-segment Elevation Acute Coronary Syndromes

Definitions, pathophysiology and epidemiology
• The universal definition for acute myocardial infarction is adopted.
Diagnosis
• An ultrarapid algorithm for the evaluation of chest pain, based on 2 determinations of high-sensitivity troponin separated by 1 h, is introduced, and the previous algorithm, involving 2 determinations separated by 3 h, remains in use (I-B) .
Risk assessment and outcomes
• Formal risk assessment with standardized scoring systems continue to be recommended (I-B). The class of recommendation of the CRUSADE score calculation has been lowered to IIb-B. • The recommended hospital unit to which the patient should be admitted is indicated (I-C). • It is recommended that all the patients with NSTEACS be admitted to a monitored unit (I-C).
Platelet inhibition
• The recommendation of ticagrelor is maintained, in the absence of contraindications, for patients with intermediate-to-high risk for ischemic events, regardless of the initial management strategy (I-B). • The recommendation of prasugrel is maintained for patients with known coronary anatomy, and PCI is indicated (I-B). Clopidogrel is still recommended for patients who need oral anticoagulation but cannot take ticagrelor or prasugrel (I-B). • The recommended duration of dual antiplatelet therapy in the absence of contraindications is 12 months (I-A); shortening or prolonging it could be considered, depending on the ischemic and bleeding risk (IIb-A). • If P2Y inhibitor discontinuation is necessary, it can be considered no sooner than 1 month after implantation of a bare-metal stent and no sooner than 3 months after implantation of a new-generation drug-eluting stent (IIb-C). • The use of GPIIb/IIIa inhibitors is restricted to the catheterization laboratory and in specific situations (IIa-C). Its use prior to coronary angiography is contraindicated (III-A). • Cangrelor is now recommended as a rapid-acting, and very transient, intravenous antiplatelet agent (IIb-A).
Anticoagulation
• The doses of parenteral anticoagulants are given for patients with normal renal function and renal failure. • Both enoxaparin and unfractionated heparin are class I-B recommendations when fondaparinux is not available. • The class I-B recommendation of bivalirudin for patients with high bleeding risk, and indication for an urgent or early invasive strategy, has been deleted. • The use of rivaroxaban (IIb-B), together with aspirin and clopidogrel, can be considered for patients without a history of stroke or transient stroke and are at high ischemic risk and low bleeding risk, after interruption of parenteral anticoagulation.
Management of antiplatelet therapy in patients receiving oral anticoagulation
• For the first time, a specific section is included for patients of this type. • There is consensus on the benefit of anticoagulation therapy at discharge for most patients, but the duration of triple therapy should be minimized. • The use of the new antiplatelet agents, ticagrelor and prasugrel, is not recommended as part of triple therapy (III-C). • The duration of dual antiplatelet therapy can be shortened with the third-generation drug-eluting stents (IIb-A).
Management of acute bleeding complications
• A series of strategies to reduce bleeding risk in patients undergoing PCI is described. • The Appendix provides general measures and practical recommendations for the management of bleeding and the treatment of bleeding associated with different drugs; prothrombin complex is often recommended. • Recommendations to restrict transfusions (IIb-C) for anemic patients (hematocrit < 25% or hemoglobin < 7 g/dL).
Invasive coronary angiography and revascularization
• Patients are classified into 4 risk categories with different timings for the invasive strategy: immediate (< 2 h), early (< 24 h), delayed (< 72 h) or elective (I-A/I-C). • Clear recommendations are given on antiplatelet therapy before and after surgical revascularization. • Radial access is recommended for coronary angiography at experienced centers (I-A). • The new-generation drug-eluting stents are recommended (I-A). • The consideration of the new-generation drug-eluting stents as an alternative to bare-metal stents is accepted for patients scheduled to receive dual antiplatelet therapy for no longer than 1 month (IIb-B). • For patients with multivessel disease, it is recommended that the revascularization strategy be chosen according to the clinical and angiographic features and in accordance with the protocol of the local Heart Team (I-C).
Special populations and conditions
• The section on sex-specific management of the patients has been deleted.
Long-term management
• The consideration of the addition of a second lipid-lowering drug (ezetimibe) is recommended if LDL-C is ≥ 70 mg/dL with the maximum tolerated statin doses (IIa-B).

ESC, European Society of Cardiology; GP, glycoprotein; LDL-C, low-density lipoprotein cholesterol; NSTEACS, non–ST-elevation acute coronary syndrome; PCI, percutaneous coronary intervention.

The 0 h/3 h algorithm has been retained (2 high-sensitivity troponin assays separated by a 3-hour interval) and the ultrarapid 0 h/1 h algorithm has been introduced (2 assays separated by 1 hour) to rule-in or rule out AMI. These algorithms have an excellent negative predictive value (around 98%) and a lower positive predictive value (75%-80%).[2] Some studies report that the limit of the 99th percentile is too high to rule out AMI and recommend troponin levels as low as the limit of detection for this purpose. The cut-off points should be optimized according to each reagent and according to the methodology of each hospital. The 0 h/1 h algorithm is unreliable in patients presenting very early (< 1 hour from chest pain onset) and there is a need for more information on the prognostic value of both algorithms. That is to say, irrespective of the diagnostic label, it is crucial to know whether direct hospital discharge is safe. As mentioned in the guidelines, the algorithms should only be used in combination with the available clinical information, including an analysis of the pain characteristics, risk factors and the electrocardiogram (ECG) results.

Figure 2 of the guidelines indicates the possibility of direct discharge for certain patients. However, the text mentions that those without signs of ischemia on ECG and with normal troponin levels, who have been asymptomatic for several hours after the index pain, are candidates for a noninvasive test for ischemia or noninvasive coronary angiography by multidetector computed tomography (MDCT). Multidetector computed tomography has a high negative predictive value, but the clinical context should be considered in its interpretation, because it may lead to an overuse of invasive coronary angiography and revascularization.[4] It is not clear when a stress