The Long-Awaited American ACS Guideline

Closer to a Universal Document

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Clinical practice guidelines are among the most impactful documents worldwide. Their impact comes not only from the vast readership and extremely high quotation, but more importantly from the undoubtful influence on patient care. The lives of millions of people around the world benefit from implementing the recommendations presented in guidelines. Therefore, releasing a guideline document is a huge responsibility for the scientific organizations endorsing them, as well as for the writing committee that works very hard (nonpaid) with the aim of producing the most evidence-based, balanced, and high-quality document. The present JACC dedicated issue is devoted to the recently released 2025 ACC/AHA/ACEP/NAEMSP/SCAI Guideline for the Management of Patients with Acute Coronary Syndromes (ACS).1 The new guideline represents not only a long-overdue update, but also a meaningful step toward global alignment in ACS care. ACS (encompassing acute myocardial infarction with or without ST-segment elevation [ST-segment elevation myocardial infarction (STEMI) and non– ST-segment elevation myocardial infarction (NSTEMI)] and unstable angina) is a life-threatening condition affecting millions of people worldwide.2 The great development of diagnostic and therapeutic interventions in the previous decades has resulted in a significant reduction of ACS-related short-term mortality. Yet, the incidence is still very high (>1.5 million U.S. citizens experience an ACS every year), and the long-term morbimortality is still high, affecting individuals and health care systems.3 Therefore, although all clinical practice guidelines are very relevant, the epidemiology of ACS makes this one among those of the greatest relevance. Given the magnificent advances in the care of ACS patients, reflected by the innumerable well-designed clinical trials published in the previous decade, the lack of a renewed guideline for the management of ACS (or any of its clinical presentations, STEMI or non–STsegment elevation [NSTE]-ACS) was a matter of critique to the American guideline publications/update scheme during the

previous years. The previous American guideline for the treatment of patients with STEMI was 2013 (with a focused update in 2015), and 2014 for NSTE-ACS. Although it is true that some guideline documents touched aspects related to treatment of ACS (eg, dual antiplatelet therapy, chest pain, coronary revascularization), a formal document was absent. This is in contrast to the position of the European Society of Cardiology (ESC), which has had a much more frequent release of guidelines in the topic (2012 STEMI, 2015 NSTE-ACS, 2017 STEMI, 2020 NSTE-ACS, 2023 ACS, and 2027 ACS [scheduled]). The current document was long-awaited and met the expectations because it updated all relevant aspects to the care of the wide spectrum of ACS. The obvious benchmark for this document is the most recent ESC ACS guidelines (2023),4 and it is important to compare them to evaluate whether care of patients in the United States and Europe significantly differs. The first commonality between the American and ESC documents is that the approach at both sides of the Atlantic is to consider ACS a single entity with different forms of presentation (STEMI, NSTEMI, or unstable angina), but with very similar diagnostic and therapeutic actions. The timing for invasive strategy differs according to the individual risk of patients, but the rest of management is very similar. This approach makes sense from the biological and practical aspects, and reduces potential discrepancies caused by different years of publications. The methodology followed by the American and ESC guidelines has been slightly different. This is exemplified by the way Level of Evidence (LOE) is categorized. In the ESC guidelines, 3 LOEs (A, B, and C) are presented, whereas for the ACC guidelines, LOEs B and C are further subdivided according to the supporting evidence. Of note, the ESC has recently presented a renewed LOE methodology,5 which seems to be closer to the American one. Still, the ESC ACS guidelines devote more space to explain to the readership why some positions were taken, while the American one is less explanatory. A paradigmatic example is the recommendation of the P2Y12 inhibitor of choice in ACS patients proceeding to PCI: the ESC guideline recommend prasugrel over ticagrelor based on the ISAR REACT 5 (Intracoronary Stenting and Antithrombotic Regimen: Rapid Early Action for Coronary Treatment) trial, whereas for the American guideline, both agents are equally recommended. ISAR REACT 5 is the only randomized, adequately powered, headto-head comparison trial (4,000 patients with myocardial infarction) and showed that, compared with ticagrelor, prasugrel was associated with a significant reduction in “death, infarction or stroke” at 12 months.6 Although the ISAR REACT 5 trial is presented in the American guideline, no explanation is given as to why it did not affect the recommendation of prasugrel in reference to ticagrelor. There are potential fair points that could have driven the writing committee to take this decision (eg, avoid conflicts with other recommendations that specifically present ticagrelor, like abbreviation strategies, open-label nature, and crossovers in the trial, patients enrolled in 1 single country, and so on). Not providing this explanation can lead to speculations of other reasons for this decision, especially given that the ESC guidelines took a different approach. Explanations for these decisions increase engagement of the community and gets away from a paternalistic approach.

The explanations for the rationale driving the writing committee to some recommendations is very welcome by readers and clinicians, especially when referring to controversial topics. In line with this, the ESC guidelines are released during the annual congress, and the writing committee interacts with the audience, engaging them more with these documents. Presentation of guidelines in a major congress not only increases visibility of these documents, but also allows for parallel sessions dedicated to hot topics dealt with in the guidelines. In addition, attendees from other regions get more exposure to guidelines and this increases the global uptake of guidelines. A dedicated paper presenting similarities and differences between the 2025 American and the 2023 ESC ACS guidelines is published in JACC. 7 Therefore, we will not dedicate space for this matter. We only want to highlight that, overall, there is a satisfying alignment between both documents. Of note, both documents recommend 12 months of dual antiplatelet therapy as the default strategy for ACS patients and present alternative strategies (ie, abbreviation of dual antiplatelet therapy) to reduce bleeding risk. This aspect has been a matter of intense debate,8 and the similar position of both documents is reassuring for the clinical community. This is especially relevant because contradictory messages between American and ESC guidelines would come with important disparities in care and potential harm for patients. Another common aspect of both guidelines is that patients took an active part in the document's preparation. Both the ESC and American ACS guideline incorporated writing committee members from other regions, pointing towards a global alignment in the care of patients. One aspect well covered in the ESC ACS guidelines to guarantee a global cover is to present an executive document dedicated to the adaptation of the ACS guidelines to low-resource settings (including low- and middleincome countries).9 Overall, the similar approach of the 2 documents makes us speculate whether a joint document endorsed by scientific societies across the Atlantic will ever be possible. This effort will benefit clinicians and, more importantly, patients across the globe. As presented here and elsewhere, the overall approach and particular recommendations in the American and ESC ACS guidelines were in general well aligned without major discrepancies. The methodologies are becoming more similar, and participation of different stakeholders is present in both. A future universal guideline is maybe a dream, but certainly today we are closer than ever.

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