Comparison of ESC and ACC/AHA guidelines for the diagnosis and management of patients with stable coronary heart disease: Are the differences clinically relevant? An American perspective

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This issue of the journal features a paper by Joseph et al.[1] which is the latest entry in the series of articles entitled ''Guidelines in Review''. This editorial is intended to provide an American perspective on the clinically relevant differences between the ESC and ACC/AHA Guidelines for the diagnosis and management of patients with stable ischemic heart disease. Joseph et al have done an excellent job of succinctly summarizing the many recommendations from these guidelines that are relevant to imaging in a series of 6 tables and 2 figures, despite the different organizational structures and wording used by the 2 guidelines to present recommendations. This editorial will provide my own personal perspective on the clinically relevant differences between the 2 guidelines. However, I would encourage the reader to carefully review the tables and figures in Joseph et al on their own, as their personal perspective on what is most relevant to their clinical practice which may well differ from mine.

Many of the recommendations that appear in the guidelines for stable coronary artery disease also appear in separate guidelines for revascularization. The Guidelines in Review series has already published a paper on the guidelines for myocardial revascularization,[2] along with two excellent editorials that provide a European perspective[3] and an American perspective[4] on those guidelines. Both of these editorials include comments about the recommendations for diagnostic testing, which by necessity overlap with mine.

As previously described,[3] the ESC and ACC/AHA Guidelines satisfy somewhat different needs. The ESC Guidelines must cover more than 30 different countries and unique health care systems. Although the US practice of medicine is certainly not homogeneous, the overall differences between individual states and regions in this country are much smaller than the differences in Europe. The ESC guideline process involves review by multiple national societies. The ACC/AHA guideline reviewers are generally more aligned in their perspective of US medicine. Both guidelines processes involve evidence review. However, the evidence review process for the ACC/AHA Guidelines has become much more rigorous in recent years, as there is now a separate systematic evidence review committee that examines key questions for each guideline. This independent process was instituted by the ACC/AHA in response to the recommendations from two separate Institute of Medicine committees—one focused on trustworthiness of clinical practice guidelines; the other, focused on systematic evidence reviews. The ACC/AHA Guideline Task Force carefully reviewed all of these recommendations and modified the ACC/AHA process.[5]

I will consider the tables that appear in Joseph et al, beginning with Table 1 (and Figure 1) regarding stress testing for diagnosis.

There are several clinically relevant differences between the guidelines in this table. The first is the different ways that the guidelines choose to address

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patients with a low pre-test probability. The ESC Guidelines urge consideration of non-cardiac causes of chest pain in these patients. In contrast, the ACC/AHA Guidelines have several class IIb recommendations for patients with a low pre-test probability who ''require testing''. These recommendations reflect the common practice in the US to perform testing on such patients, although Bayes' theorem indicates that such testing is unlikely to be beneficial. Positive tests will inevitably occur in such patients, due to the imperfect specificity of our tests, and are very likely to be ''false-positives''. These ''false-positives'' often lead to further unnecessary testing, and patient confusion rather than reassurance.

The second clinically relevant difference between the guidelines deals with the thresholds for pre-test probability. The exact thresholds for ''low probability'' and ''high probability'' are uncertain. The original ACC/AHA Guideline on stable angina[6] used 10% and 90% thresholds, respectively, for these two categories. The ESC Guidelines have favored 15% and 85% thresholds. This relatively minor difference is less important than how these probabilities are determined. The ACC/AHA Guidelines have favored the early estimates of Diamond and Forrester,[7] modified by the influence of risk factors(particularly, diabetes mellitus).[8] However, in recent years, a consortium of European centers[9] have suggested an important revision of these estimates, which is incorporated in the ESC Guidelines. This European formulation reclassifies many patients; in particular, very few women have a high pre-test probability. This change likely reflects a number of influences, including the declining overall population prevalence of hypertension, hyperlipidemia, and tobacco use.[10]

The third clinically relevant difference between the guidelines with respect to diagnosis is the specific Class III recommendation in the ACC/AHA Guidelines regarding the use of pharmacologic stress testing in patients who are able to exercise. Although both guidelines recommend exercise as the preferred stress modality in patients who can exercise, the inclusion of this Class III recommendation in the ACC/AHA Guidelines reflect a general impression that pharmacologic stress testing is often used in the United States in patients who are able to exercise, as clinicians find it too difficult to take the time to estimate the patient's ability to exercise. This unfortunate trend in clinical practice merits this Class III recommendation.

Table 2 describes the use of CCTA and the diagnosis of coronary artery disease. There are two clinically relevant differences. In the ESC Guidelines, CCTA is given a Class IIa recommendation for diagnosis as an alternative to stress imaging in patients with low-intermediate pre-test probability. The ACC/AHA Guidelines give a similar Class IIa recommendation if the patient is unable to exercise, but only give a Class IIb recommendation if the patient is able to exercise. This is not a minor difference, as many patients are able to exercise. It reflects a concern at the time the ACC/AHA Guidelines were developed that there was early evidence in the United States that the performance of CCTA led to an increased rate of invasive angiography and subsequent revascularization.[11] That early evidence has been confirmed subsequently in the PROMISE Trial.[12] Both the PROMISE and SCOT-HEART Trials[13] were published after these ESC and ACC/AHA Guidelines were developed. It will be interesting to observe the subsequent changes that are made in these guidelines in response to the publication of these two trials. It is worth noting that the different results in the two trials reflect a difference in behavior of physicians in the United Kingdom and in that United States in response to abnormalities detected by CCTA.

The second clinically relevant difference regarding CCTA for diagnosis is the inclusion of two separate Class IIb recommendations in the ACC/AHA Guidelines regarding the use of calcium scoring. These recommendations reflect the use of calcium scoring by some clinicians for decision making in symptomatic patients, even though the evidence supporting that use was very limited at the time these guidelines were developed. This is another area where there is now more current evidence, including a publication from the PROMISE Trial.[14] The ACC/AHA Guideline process will need to consider this new evidence, and decide whether to modify its recommendations and text based on these emerging data.

Table 3 describes the use of stress testing and CCTA for risk stratification. The recommendations for CCTA are more detailed in the ACC/AHA document. Rather than the broad Class IIa recommendation assigned in the ESC Guidelines, the ACC/AHA Guidelines identify 2 categories of patients for whom CCTA has a weaker IIb recommendation – those who can exercise but have an interpretable ECG, those who cannot undergo stress imaging, and as an alternative to invasive coronary angiography when functional testing indicates moderate to high risk of cardiac events. These Class IIb recommendations reflect the concern described previously that CCTA in the US has led to an increased rate of invasive angiography and subsequent revascularization. Subsequent revisions of both the ESC and ACC/AHA Guidelines will reflect the new evidence from the PROMISE and SCOT-HEART Trials on this topic.

One of the most relevant differences between the ESC and ACC/AHA Guidelines for risk stratification is not obvious from review of Table 3, i.e., how to

interpret the results of a stress test to decide that early invasive angiography and/or revascularization is warranted. The ESC Guidelines emphasize the identification of > 10% ischemia by stress imaging, but misinterpret the available evidence for SPECT imaging. As detailed in a 2015 review,[15] the ESC Guidelines focus only on the extent of ischemia, rather than the extent and severity of ischemia, which was the focus of previous SPECT studies. The ACC/AHA Guidelines do not make this error. However, they do not provide clear guidance for interpretation of the exercise ECG. The ACC/AHA Guidelines include a figure from the landmark paper by Lauer,[16] but refer to high-risk criteria that are based on ST segment change and chest pain, components of the Duke treadmill score[17] which were not found to be significant in the thorough (both retrospective and prospective) analysis by Lauer.

Table 4 describes the use of stress testing and/or CCTA for re-assessment of patients during follow-up. The most clinically relevant difference in this table with respect to follow-up testing in symptomatic patients is a Class IIb recommendation for the use of CCTA in the ACC/AHA Guideline. This recommendation presumably reflects a desire to ''specify boundaries'' for the use of CCTA to avoid its overuse and any downstream increase in invasive coronary angiography and revascularization.

With respect to asymptomatic patients or patients with stable symptoms, the ESC Guidelines include a Class IIb recommendation for re-assessment in asymptomatic patients after the ''warranty period'' has expired. In contrast, the ACC/AHA recommendations include a stronger Class III recommendation against stress imaging or CCTA at follow-up intervals of less than 5 years post-CABG or 2-years post PCI. This clinically relevant difference reflects the single published study regarding the use of the warranty period by US clinicians[18] which found that follow-up testing was frequently performed before the expiration of the warranty period in patients *without* known coronary artery disease, and well after the expiration of the warranty period in patients *with* known coronary artery disease. This published experience suggests that US clinicians do not properly apply the warranty period concept.

Table 5, which addresses recommendations for the use of resting echocardiography, demonstrates clinically relevant differences between the ESC and the ACC/AHA Guidelines. The ESC Guidelines list a broad Class I recommendation for echocardiography. The ACC/AHA Guidelines restrict the Class I recommendation to patients with ECG Q waves, a history of prior myocardial infarction, symptoms or signs of heart failure, complex ventricular arrhythmias, or an undiagnosed heart murmur. The ACC/AHA Guidelines include a weaker Class IIb recommendation for patients with hypertension or diabetes and an abnormal ECG. The more restrictive ACC/AHA recommendation is founded on strong evidence, as multiple previous studies have shown a very low yield for the assessment of left ventricular function in patients with a normal resting ECG. The earlier studies on this subject, summarized in the original 1998 ACC/AHA Stable Angina Guideline,[6] employed a variety of modalities—first-pass radionuclide angiography, gated radionuclide angiography, echocardiography, and contrast ventriculography. Regardless of the imaging method, patients with a normal ECG had a > 95% prevalence of normal left ventricular function. To avoid unnecessary imaging, a Class III recommendation for patients with a normal ECG and no other indication for echocardiography has been a consistent feature of the ACC/AHA Guidelines.

Two recent studies examined the compliance over a five year period with this Class III recommendation in both local patients and referral patients.[19,20] The findings in the two studies were remarkably consistent. Among patients with chest pain and a normal resting ECG, relatively few patients had an echocardiogram in the absence of other indications. In those who did, the rate of abnormal findings was remarkably low and had little impact on clinical management. In a few patients, abnormal findings on the resting echocardiogram performed in violation of the Class III recommendation led to additional testing using other modalities which failed to confirm the abnormal echocardiographic finding. Thus, two recent contemporary studies have reaffirmed the value of the original long-standing Class III recommendation in the ACC/AHA Guidelines.

Table 6 describes the investigation of patients with suspected microvascular or vasospastic angina. The ESC Guidelines have a number of recommendations; the ACC/AHA Guidelines do not have any recommendations for these patients. These differences are certainly clinically relevant. However, the true prevalence of these disorders in general patient populations is not known, as the published data is restricted to a limited number of academic medical centers with a specific interest in such patients. For microvascular angina, the ESC Guidelines define a Class IIb recommendation for ''intracoronary acetylcholine adenosine with Doppler measurements… to assess coronary flow reserve and to detect vasospasm''. This time-consuming protocol is not widely available. The published experience from the Mayo Clinic is the largest available series of such patients.[21] It comprised 1,552 patients over a 20 year period. Most of these highly selected patients (about 1.5 patients per week over 20 years) were referred from outside Mayo after a coronary angiogram failed to demonstrate obstructive disease. The level of evidence

cited for this recommendation is expert opinion, which undoubtedly reflects the presence of one of the recognized international experts in this area on the ESC Guideline committee. Recognition of the importance of this issue in the US prompted a 2016 workshop that was jointly sponsored by the National Institutes of Health, the ACC and the AHA. Proceedings of that INOCA workshop were published in 2017[22] and provide a very thoughtful review of the published data and the unresolved questions.

The ESC Guidelines also include specific recommendations for the evaluation of patients with suspected vasospastic angina, including an ECG during angina, coronary angiography to determine the extent of CAD in patients with a characteristic clinical pattern, and intracoronary provocation tests to identify the type of spasm. All of these recommendations are only supported by expert opinion. I suspect that the presence of a recognized international expert on the ESC committee again played a role in their inclusion in the ESC guidelines. I doubt that anyone on the ACC/AHA Guideline committee would dispute the potential value of these steps in these highly selected patients. Their omission from the ACC/AHA Guideline likely reflects the absence of definitive evidence regarding the prevalence of this disorder and the absence of any randomized trial evidence demonstrating the efficacy of the commonly used empirical therapies. The previously cited INOCA workshop paper had very specific criteria for the diagnosis of coronary vasospasm, which are rarely met in clinical practice in the United States.

I hope that this editorial has highlighted some of the clinical relevant differences that are evident in the Guidelines in Review paper by Joseph et al. Joseph et al did an excellent job. Interested clinicians should carefully review their paper and this editorial with respect to their own clinical practice. Readers are encouraged to monitor further revisions in these guidelines, reflecting the emerging data from the PROMISE and SCOT-HEART Trials, as well as the INOCA workshop.

Disclosure

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