

Artículo de Revisión

Chronic coronary syndromes – guideline changes and a new nomenclature

Síndromes coronarios crónicos: Modificaciones en las guías y una nueva nomenclatura

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ABSTRACT

Our understanding of the pathogenesis, clinical presentation, diagnosis, and management of angina pectoris has evolved substantially over the past few decades. Newer international guidelines have recently been published that provide recommendations for the diagnosis and management of ischaemic syndromes which are aligned with the advances in the pathogenesis of ischaemic myocardial syndromes. In parallel to those very welcome updates of the European guidelines I argue in this manuscript that nomenclature changes are required to better reflect the large spectrum of phenotypes and clinical presentations that come to our attention in clinical practice and currently grouped under the term chronic coronary syndromes. The latter term does not truly reflect the important contribution that non-obstructive coronary causes and non-vascular causes of both myocardial ischaemia and myocardial infarction make to the pathogenesis of ischaemic heart syndromes. This manuscript represents a viewpoint about the need for a more comprehensive and accurate nomenclature that helps clinicians to plan stratified treatments based on specific pathogenic mechanisms rather than focusing on epicardial coronary artery obstructions as the key mechanism underlying myocardial ischaemia.

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RESUMEN

Nuestra comprensión de la patogénesis, presentación clínica, diagnóstico y tratamiento de la angina de pecho ha avanzado considerablemente en las últimas décadas. Se han publicado recientemente nuevas guías con recomendaciones para el diagnóstico y tratamiento de síndromes isquémicos, que siguen los avances realizados en el conocimiento de la patogénesis de la isquemia miocárdica. De forma simultánea a tales actualizaciones de las guías europeas, muy bienvenidas, en este manuscrito propongo que se precisen cambios de nomenclatura para que se refleje mejor el extenso rango de fenotipos y presentaciones clínicas que nos llaman la atención en la práctica clínica y que actualmente se agrupan bajo el término síndromes coronarios crónicos. Este término no refleja verdaderamente la importante contribución que las causas coronarias no obstructivas y las causas no vasculares, tanto de la isquemia miocárdica como del infarto de miocardio, ejercen sobre la patogénesis de la cardiopatía isquémica. Este manuscrito presenta el punto de vista de que se precisa una nomenclatura más integral y precisa que ayude a los clínicos a planificar tratamientos estratificados en base a mecanismos patogénicos específicos, antes que enfocarse en las obstrucciones coronarias epicárdicas como el mecanismo clave que subyace a la isquemia miocárdica.

Chronic coronary syndromes (CCS) affect many people worldwide and the number continues to rise due to many factors that include, among others, improved survival after myocardial infarction, better diagnostic tools, and increased awareness among patients and general practitioners.

The new 2024 ESC Guidelines have highlighted the importance of different mechanisms that lead to CCS over and above coronary atherosclerotic obstructions and the role of personalised risk stratification and management¹. Patients with angina despite angiographically normal coronary ar-

teries (ANOCA/INOCA) now feature with class I indications in the 2024 guidelines regarding diagnostic tests required to identify these conditions and the implementation of stratified management strategies. Indeed, acknowledging the findings by different investigators and large trials regarding the mechanisms responsible for angina pectoris the 2024 ESC Guidelines on the management of CCS have incorporated new recommendations regarding the pathophysiological role of both epicardial coronary arteries and the coronary microcirculation of the heart, diagnostic strategies to investigate myocardial ischaemia and microvascular dysfunction, risk stratification of angina patients, and both the diagnosis and the management of vasospastic syndromes^{1,2,3}.

Additions to the 2024 ESC guidelines on the management of CCS represent a long overdue clinical need, given the high prevalence of ANOCA/INOCA worldwide. The 2019 CCS ESC guidelines reported that among patients with typical angina aged 50–59 years, 68% of men and 87% of women did not have obstructive coronary stenoses, and the Coronary Microvascular Angina (CorMicA) trial showed that approximately 45% of patients presenting with stable angina did not have CAD at angiography^{4,5}. Along these lines, a US registry of 400,000 patients with suspected CAD referred to diagnostic coronary angiography only 38% of patients had obstructive CAD⁶. In INOCA/ANOCA patients' myocardial ischaemic syndromes are caused by coronary artery spasm, a vasodilatory abnormality of the coronary microcirculation or a combination of both. Identifying these phenotypes (clinical presentations) is of paramount importance for treatment and the 2024 ESC guidelines recommend that symptomatic patients with ANOCA/INOCA undergo invasive coronary functional testing to identify the underlying pathophysiological "endotypes" and to guide medical therapy¹.

The newer ESC recommendations for the diagnosis and management of CCS can have a major clinical impact but so would an update of the nomenclature that is currently used to refer to myocardial ischaemia syndromes. Recently, we argued that the clinical terminology needs changing to more accurately define and classify chronic ischaemic heart disease conditions⁷. Importantly, consensus has been reached among major international cardiovascular societies regarding the classification of acute coronary syndromes (ACS) a similar agreement, however, would be necessary regarding the nomenclature used to define chronic stable manifestations of myocardial ischaemia. At present, major American and European Cardiovascular Societies and cardiologists around the globe use many different terminologies to refer to stable, non-acute myocardial ischaemia syndromes, i.e. 'stable coronary artery disease' (CAD), 'stable ischaemic heart disease' (SIHD), 'chronic coronary syndromes' (CCS), and 'chronic coronary disease' (CCD). This lack of uniformity conspires against the understanding of mechanisms and clinical implications and management of these more stable conditions. Indeed, while the 2019 ESC gui-

delines introduced the term "CCS" to align it with the well accepted term "acute coronary syndrome - ACS" to identify acute myocardial ischaemia syndromes, the 2023 American guidelines proposed the use of the term "chronic coronary disease" (CCD)^{4,8}. Although these discrepancies may look irrelevant, they can cause confusion and fail to define stable conditions in a comprehensive and accurate fashion. In a recent article by Boden et al we highlighted the need to achieve a more uniform, more widely accepted terminology that helps clinician to identify the different patient subgroups and mechanisms currently encompassed under the flawed term "coronary artery disease" that focuses almost exclusively on obstructive coronary atherosclerosis as the main cause of myocardial ischaemia and angina⁷.

Although obstructive CAD has for decades been viewed as the most common cause of angina, strong and ever-growing scientific evidence confirmed that there are many important *non-obstructive* causes of myocardial ischaemia that cannot be easily included under the broad terms CCS or CCD supported by international societies. The reason being that coronary epicardial obstructions are not the only cause of myocardial ischaemia or MI, which can occur in the presence and in the absence of obstructive CAD⁹. We have recently argued in favour of "a practical, accurate nomenclature that should fully reflect the totality of potential obstructive and non-obstructive causes of ischaemia occurring in both the acute and the non-acute clinical settings"⁷.

A new, accurate, contemporary classification that is comprehensive, inclusive, based on pathogenesis, and clinically relevant should allow not only the accurate identification of pathogenic subgroups but also help to manage these patients in a personalised fashion.

Myocardial ischaemia, and the myocardium at the centre of the definition and moving away from a terminology based only on "coronary" and "disease".

Myocardial ischaemia represents the final common pathway by which different mechanisms lead to symptoms, myocardial damage, and major adverse cardiovascular events. While obstructive CAD is a very important cause of myocardial ischaemia in acute and chronic settings, keeping the focus only on epicardial CAD has slowed down progress in the understanding and management of myocardial ischemia for decades. As myocardial ischaemia can be triggered by a multitude of mechanisms other than obstructive CAD it is only logical that the nomenclature accurately reflects the situation.

Moving away from a terminology that endorses the concept that obstructive CAD is the only reasonable cause of myocardial ischaemia is vital at this point. The use of terms such as 'disease' or 'lesion' immediately draws attention towards epicardial coronary artery stenoses that need to be treated by revascularisation. The new terminology should address both coronary and non-coronary causes of myocardial ischaemia. The term 'ischaemic syndrome', as proposed recently by our group, better indicates that angina and

ischaemia can have many pathogenetic causes compared with the term ‘coronary disease’. Incorporating the newly proposed terminology does not mean to negate the extremely important role of epicardial coronary obstruction or coronary stenoses as a cause of ACS or more chronic clinical presentations⁷. Our proposed changes aim to highlight the fact that the widely used term ‘coronary’ does not include the many *non-coronary* causes of myocardial ischaemia, such as microvascular dysfunction, extramural microcirculatory compression, microvascular embolization, capillary rarefaction, and myocardial oxygen diffusion abnormalities. Moving away from the term “coronary” and adopting the term “ischaemic syndrome” may help cardiologists to think about other important causes of angina and ischaemia that we often fail to consider. This may also help devising more effective diagnostic strategies that incorporate functional tests rather than just relying on anatomical tests such as coronary computed tomography angiography (CCTA). Currently proposed strategies based on CCTA often fail to identify INOCA patients, as individuals with no obstructive coronary arteries are usually reassured without further tests or are considered to have “non-cardiac” pains. Moreover, the treatment of patients with stable myocardial ischaemia would also benefit from such an approach, as treatments would then be directed to the pathogenic or causal mechanisms.

WHY A NEW NOMENCLATURE IS NEEDED

As mentioned above, in a recent paper jointly published in the European Heart Journal and Circulation we argued that “a classification system that uses ‘chronic’ or ‘stable’ as the contrasting description of ‘acute’ does not accurately depict the full measure of subsequent cardiovascular risk associated with the condition, and likewise may perhaps convey an inadvertent misperception of a clinically benign condition”⁷. We, therefore, propose the term “*myocardial ischaemic syndromes*” (MIS) as a more accurately way to encompass the diverse clinical presentations of myocardial ischaemia and the diverse mechanisms that can cause myocardial ischaemia in the acute and non-acute settings. The proposed new classification system is as follows: ‘myocardial ischaemic syndromes’ encompassing subcategories such as ‘acute myocardial ischaemic syndromes’ (AMIS) and ‘non-acute myocardial ischaemic syndromes’ (NAMIS). We prefer the term “non-acute” to “chronic” as we believe that in the medical world the word “chronic” refers to a condition 3 months or longer in duration that may get worse over time and can be controlled but not cured. Obstructive CAD may fall under this category but not necessarily all other forms of myocardial ischaemia can be encompassed by this terminology. Importantly, we proposed to retain ‘ACS’ as a subcategory of AMIS which in turn will encompass STEMI, NSTEMI, and unstable angina, and

identify both epicardial coronary artery causes and non-coronary causes (MINOCA). Patients with chronic angina and myocardial ischaemia who have obstructive, flow-limiting epicardial coronary stenoses would be classified as having a NAMIS due to obstructive coronary disease, and those with chronic angina and/or myocardial ischaemia caused by mechanisms other than obstructive CAD will be called NAMIS, which will include stable obstructive CAD and stable angina caused by non-obstructed arteries, or INOCA.

We should not forget that non-obstructive functional mechanisms of ischaemia often co-exist with anatomic obstructive CAD, hence ischaemia of microvascular origin should not be considered to exclude a co-existing obstructive problem and *vice versa*, the presence of obstructive CAD does not exclude the possibility of microvascular dysfunction as a synergistic trigger of ischaemia in a given individual.

In conclusion, our proposed classification into ‘AMIS’ and ‘NAMIS’ should help providing greater conceptual clarity and unify what can at present be considered to represent a competing and rather confusing nomenclature. By better harmonizing different pathophysiologic causes of angina, myocardial ischaemia and MI, the newly proposed nomenclature should allow more accurate diagnostic testing and stratified therapeutic strategies.

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