Advanced imaging in the diagnosis of cardiovascular diseases: the "ongoing" future

I am very pleased to write the Editorial for this special Issue entitled "Advanced Imaging in the diagnosis of Cardiovascular Diseases" published by *Cardiovascular Diagnosis and Therapy* Journal because this topic represents a fundamental area of intersection between advanced research in the field of imaging and the need of early identification of the atherosclerotic disease, the underlying process of two of the most important causes of death worldwide: ischemic stroke and myocardial infarction.

Atherosclerosis has a high prevalence in western countries, with values up to 75% of men and 62% of women aged 65 (1). Despite significant advances in treatment, current conventional screening and diagnostic methods are insufficient to identify the victims before the event occurs even if in the last years the recognition of the role of the vulnerable plaque has opened new windows of opportunity in the field of cardiovascular medicine. The two vascular territories responsible for most of the cardiovascular events are the coronary arterial tree and extracranial carotid arteries. In both carotid and coronary arteries, the rupture of the plaque is considered the cause of the pathological cascade which determines ischemic stroke and myocardial infarction.

A better understanding of the pathophysiology of atherosclerosis has created the need for dedicated imaging and, in fact, much progress has been made in the last 20 years. In the carotid area, The European Carotid Surgery Trial (ECST) (2) and North American Symptomatic Carotid Endarterectomy Trial (NASCET) (3) have effectively shown that carotid endarterectomy (CEA) can prevent stroke and death in symptomatic patients selected on the basis of the degree of stenosis. Conventional catheter angiography was the only imaging technique available at the time of ECTS and NASCET trials, because CT Angiography or MR Angiography were not commonplace. This determined the creation of a relatively simple and reproducible method, the percentage degree of stenosis, that could be used as cut-off to easily stratify the patients.

However, this methodology implied that the stenosis itself, not the underlying cause of the stenosis, was associated with an increased risk of stroke. This approach ignored the concept that the increased degree of stenosis is likely associated with an underlying increase in plaque volume. Angiography could provide information regarding morphological features but could not provide information on plaque composition and relative risk of rupture. However, the percent reduction in luminal diameter of the artery is still considered a dominant predictor for the stratification of the severity of atherosclerotic process (4).

Nevertheless, multiple ex-vivo studies demonstrated that, given the same degree of luminal stenosis, there are significant differences in terms of risk of plaque rupture and that these differences correlate with plaque structure. In fact, by focusing the attention on some plaque features, such as intra-plaque hemorrhage (IPH), an association was found with a significantly increased risk of plaque rupture and distal embolization. These features can nowadays be explored *in vivo* in both carotid and coronary arteries thanks to the evolution of advanced diagnostic methods (4-6), opening the potentiality to offer diagnostic information and move forward beyond the mere quantification of the degree of stenosis (7).

Computed tomography (CT) (8-10) and magnetic resonance (MR) (11-13) are the main non-invasive tools for plaque analysis both in carotid and coronary arteries, whereas other methods such as optical coherence tomography (OCT), and Intravascular Ultrasound (IVUS) are the main invasive intravascular methods for the assessment of coronary atherosclerosis; conventional Doppler-Ultrasound (US) plays also a major role in the assessment carotid artery atherosclerotic disease (14,15). A minor, but very intriguing role, might be played by nuclear medicine techniques and in particular by Positron Emission Tomography (PET), which is the tool that at this point in time can bring us the closest to actual molecular/metabolic imaging of carotid and eventually coronary atherosclerosis (16). It is also interesting to note that there are similarities in physiopathology and imaging findings between the carotid and coronary arteries (17) and these features will be covered in this special issue.

Another important target of atherosclerosis which will be explored in this issue is the intracranial vasculature (18). Cerebral arteries represent a significant target not only for atherosclerotic process but also for inflammatory and autoimmune pathologies. It is possible to explore cerebral arteries with both CT and MR technologies but only the MR currently offers the potentialities to visualize the intracranial arterial wall with an adequate spatial and contrast resolution. This opportunity is gaining new space for MR in understating physiopathology of some ischemic strokes that in the past years were considered cryptogenic strokes (19). In this issue imaging of intracranial arteries will be also described by analyzing the impact of new and emerging technologies in MR area (20) such as the super-strength magnetic fields (7T). Among other emerging and advanced technologies, also dual-energy CT applications will be described, with particular regard to coronary imaging, where it seems that this technology could offer new and important information related to the vulnerability of the plaque (21).

Until some years ago, imaging exams were mainly "morphological exams" whereas recently we are observing a steady and continuous shift toward the "quantitative imaging" (22). Radiologists are experiencing in their activity the need and potentiality to detect and stratify pathologies according to quantitative values. One exciting field is the four-dimensional flow imaging analysis (23), an area which will be analyzed in 2 papers within the present issue, with specific attention to yet another important target of the atherosclerotic process: the aorta.

Lastly, we shall consider the ongoing revolution presently taking place in the imaging field, which is, Artificial Intelligence and its application to the detection and interpretation of the cardiovascular imaging exams (24). A growing evolution from the simple *machine learning algorithms* to the newer and more complex deep learning algorithms is adding new potentialities and also role to the AI in the daily and routine application of these process in the diagnostic day-to-day practice.

In conclusion I am deeply proud to have had the opportunity to follow this special Issue dedicated to such a fundamental topic and I am deeply indebted with the authors of the papers for the wonderful insight they have offered by showing clearly and deeply their research field, the potentialities and application of advanced imaging in the diagnosis of Cardiovascular Disease. A special thank also to Professor Paul Schoenhagen, Editor in Chief of *Cardiovascular Diagnosis and Therapy*, for inviting me to lead this special issue and for his friendship.

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