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Editorial

Recent highlights on coronary artery disease from the *International Journal of Cardiology Heart & Vasculature*

Coronary artery disease (CAD) is a leading cause of death in Western Countries. CAD has been considered as a disease mediated by aberrant lipid accumulation with subsequent injury to the cardiovascular (CV) system. Lipid content in coronary atheromatous plaques, measured by near-infrared spectroscopy (NIRS), has been demonstrated to predict the risk of future coronary events [1]. High plasma levels of lipoprotein (a) are associated with thin-cap fibro-atheroma and a worse prognosis in patients with CAD [2]. In the attempt to identify non-invasive surrogate biomarkers for lipid burden in coronary plaques, Sæther et al. reported that serum levels of lipoprotein (a) and free cholesterol in the smallest HDL sub-fractions have the strongest potential as predictors for lipid content in coronary atheromatous plaques [3]. In recent years, the research ofCAD has focused on the potential contribution of the immune system. Using a novel multiplex immunohistochemistry technique, Kimberley et al. investigated immune cells and related subsets/subpopulations of cells in the different stages of human CAD. They have profiled the individual cell types from both innate and adaptive immunity, providing insights in the overall immune landscape and the dynamic changes in immunity during the progression of CAD [4]. This study demonstrated that cardiologists and immunologists should closely collaborate to further advance our knowledge about CAD pathophysiology [5]. The knowledge generated by immune profiling in patients with CAD could promote the application of next-generation immunotherapy and foster the repurposing of old drugs in treating this condition [6], although the use of anti-inflammatory drugs in CAD has demonstrated mixed and often neutral results [7–9]. In one well-conducted meta-analysis, Siddiqui et al. found no significant differences in the risk of myocardial infarction (MI), need for percutaneous coronary intervention (PCI), or need for coronary artery bypass grafting (CABG) between patients with gout on colchicine compared to controls [10].

The opportunity of choosing targeted therapeutic strategies for patients with ischemic heart disease (IHD) represents one of the most prominent achievements in the CV field. It is known that patients with diabetes tend to develop complex multivessel CAD. To assess long-term CV outcomes in patients with diabetes and multivessel CAD treated with CABG and PCI, Jaiswal and colleagues conducted a meta-analysis demonstrating that cardiac surgery provides long-term net clinical superiority [11]. Since various conduits could be selected for CABG, Stefil et al. [12] performed a systematic review and meta-analysis comparing the use of single grafting to bilateral internal mammary (BIMA) grafting in patients with diabetes or obesity. The long-term survival was in favor of BIMA grafting at the expense of an increase in perioperative sternal wound infections [13,14]. Despite clear evidence supporting CABG as the first revascularization option in patients with diabetes and obesity, prior studies suggest that patients often have no consultation with a cardiac surgeon. Therefore, a multidisciplinary Heart Team discussion to ensure personalized decision-making and alignment between evidence and practice is clearly required [14]. Wein and colleagues reported low adherence to guidelines for patients with CAD [15]. In the last 20 years, PCI has become the treatment of choice in most cases of CAD, and several technical aspects have been demonstrated to significantly affect patient outcomes. Accordingly, a great effort has been made to improve the equipment at our disposal in the catheter lab. To overcome the side effects related to the administration of a vasodilatory drug during the application of Fractional Flow Reserve (FFR) measurements, the use of non-hyperemic pressure ratio (NHPRs) has been recently validated as a reliable alternative [16]. Among these, vessel FFR (vFFR) is a novel 3D-quantitative coronary angiography-based technology whose application in evaluating non-culprit lesion (NCL) in ST-elevation MI (STEMI) patients has been suggested as a more consistent classifier of intermediate NCL as compared to both FFR and instantaneous wave-free ratio (iFR) [17]. Since complicated lesions in the target coronary artery often hinder device delivery, contrast media could be used as a fluid lubricant to facilitate device placement [18]. The introduction of intravascular imaging including either intravascular ultrasound (IVUS) or optical coherence tomography (OCT) has been associated with improved outcomes [19]; however, these techniques remain underutilized in daily clinical practice [20]. The treatment of coronary bifurcation lesions still represents a challenge for interventional cardiologists. In this setting, Yamawaki and colleagues have reported that a wider bifurcation angle has a potential risk for the occurrence of major incomplete stent apposition after proximal optimization technique followed by short balloon dilation in the side branch in coronary bifurcation stenting [21]. Intracoronary acetylcholine (ACh) provocation test is an established method for diagnosing epicardial and microvascular vasospasms. Since ACh provocation test does not identify all patients who could benefit from appropriate therapy [22], flow-recovery time has been suggested as a parameter to identify patients with equivocal results of ACh test who may receive appropriate medical treatment to improve symptoms and quality of life [23]. The same group recently conducted a randomized, double-blind, placebo-controlled trial, which failed to demonstrate the usefulness of the endothelin-1 receptor antagonist macitentan in identifying patients with epicardial or microvascular coronary vasospasm who remain symptomatic despite background pharmacological treatment [24]. Spinal cord stimulation is a new option to treat patients with refractory angina pectoris, which has been shown to improve quality of life, reduce frequency of angina, and decrease the use of short-acting nitrates, which are frequently applied in

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this scenario [2]. Although the indication for a dual antiplatelet therapy consisting of aspirin and a strong P2Y12 inhibitor in patients undergoing PCI after acute coronary syndrome (ACS) is well consolidated, concerns were raised about the impact of renal failure on the pharmacokinetics and pharmacodynamics of ticagrelor. For this reason, Porlàn et al. performed a prospective mechanistic cohort study, which revealed no significant differences in platelet inhibition after treatment with ticagrelor in patients with different degrees of renal dysfunction [25].

There are some new developments regarding the diagnostic process and the prognostic stratification of patients with CAD. Detection of cardiac troponin is the 'gold standard' for the diagnosis of acute MI, with no notable difference in trajectories, time-to-peak or half-life between high-sensitivity troponin (hsTn) assays [26,27]. Nevertheless, there is growing interest around the use of cell-free DNA (cfDNA) as an additional reliable biomarker of myocardial injury [28]. Since the introduction of hsTn assays has shifted the diagnosis of unstable angina (UA) in favor of non-ST elevation MI (NSTEMI), Herrero-Brocal et al. performed a study to determine whether using hsTn results in medium-term prognostic differences in patients with these two conditions. While the medium-term incidence of major adverse cardiovascular events (MACE) was similar in patients with UA and NSTEMI, CV and all-cause mortality in NSTEMI patients was 2-fold higher than that of patients with UA [29]. In NSTEMI context, adequate risk assessment and subsequent clinical management are mandatory to optimize patient outcomes and the Global Registry of Acute Coronary Events (GRACE) risk score gives better risk evaluation than clinical judgment only in this setting. Since publications using East European populations are lacking, Ferencia et al. investigated the validity of the GRACE risk score in a Hungarian population, confirming the usefulness of this risk score in identifying high-risk patients with NSTEMI [30]. Although according to physicians' perception, the COVID-19 pandemic significantly affected the clinical management of CAD [31], the impact of COVID-19 pandemic on CAD prognosis remains uncertain. This was explored in NSTEMI patients by Sanjaya and colleagues; despite a prolonged door-to-wire time, no significant increase in mortality was demonstrated [32]. Several prognostic factors have been described for patients with stable CAD. Interestingly, when evaluated based on appendicular skeletal muscle mass sarcopenia has been shown to independently predict MACE and all-cause mortality [33]. Furthermore, a history of cancer and atrial fibrillation in patients with CAD is related to an increased risk of composite outcomes, including stroke, systemic thrombosis, major bleeding, all-cause death, cancer-related death, and new-onset heart failure [34]. A diagnostic method that is gaining growing importance is coronary computed tomography angiography (CCTA) [35]. It is widely used in clinical practice as a first-line test for symptomatic or asymptomatic patients at risk of obstructive CAD, allowing non-invasive assessment of CAD severity and extent. CCTA also enables the quantification of epicardial adipose tissue, which together with CAD severity, even in less advanced stage of atherosclerosis, has been demonstrated to be associated with a deterioration of the left ventricular longitudinal strain in patients with heart failure with preserved ejection fraction [36]. However, a recent study found no differences in epicardial adipose tissue volumes among patients with previous MI, stable CAD and healthy controls in an age-, sex- and BMI-balanced population without extremes of traditional CVD risk factors [37]. Cardiocirculatory arrest (CCA) may be the first clinical presentation of CAD and the appropriate management of these patients remains challenging. Targeted temperature management (TTM) has historically been recommended for out-of-hospital and in-hospital cardiac arrest patients who remain unresponsive after the return of spontaneous circulation, particularly in shockable rhythms, even if several trials failed to demonstrate clear survival benefits [38,39]. However, a recent study suggested a possible negative association between TTM and unplanned 30-day readmission in CCA survivors, thereby potentially reducing the impact and burden of increased short-term readmission in these patients [40]. In CCA survivors, the prognostic impact of left/right bundle branch block (LBBB/RBBB) in patients with no CAD has been characterised by Holm et al., who reported a high prevalence of LBBB among all CCA survivors [41]. Furthermore, LBBB patients presented with a significantly lower left ventricular ejection fraction than patients with non-L BBB, while no differences in implantable cardiac defibrillator treatment and mortality were found between LBBB and non-LBBB subtypes during follow-up [41]. Another condition known to be associated with worse outcome is Thrombolysis in Myocardial Infarction (TIMI) grade zero flow in patients with AMI. Since this condition may also feature in NSTEMI patients, Aarts and colleagues performed a single-center retrospective study that demonstrated a similar clinical outcome in NSTEMI and STEMI patients with TIMI grade zero flow [42]. Finally, the long-term consequences of AMI are determined by infarct size. To explore whether physical exercise in animals undergoing ischemia and reperfusion brings benefits the heart, the group of Carvalho de Arruda Veiga conducted a systematic review that highlighted how exercised rats subjected to ischemia and reperfusion tend to have reduced infarct size and preserved ejection fraction, with subsequent beneficial myocardial remodeling [43].

In recent years the *International Journal of Cardiology: Heart & Vasculature* has published many papers related to CAD and its complications and will continue to expand our knowledge about diagnosis, treatment, and prognosis of CAD, hoping to further serve as a publishing platform for the dissemination of new insights related to CAD and myocardial infarction.

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Declaration of competing interest

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Andrea Tedeschi
De Gasperis Cardio Center, Niguarda Hospital, Milano, Italy
Guglielmo da Saliceto Hospital, Piacenza, Italy

Enrico Ammirati*, Nicolina Conti
De Gasperis Cardio Center, Niguarda Hospital, Milano, Italy

Dobromir Dobrev
Institute of Pharmacology, West German Heart and Vascular Center, University Duisburg-Essen, Essen, Germany
Department of Integrative Physiology, Baylor College of Medicine, Houston, USA
Department of Medicine and Research Center, Montréal Heart Institute and Université de Montréal, Montréal, Canada

* Corresponding author at: Niguarda Hospital, Piazza Ospedale Maggiore 3, 20162 Milano, Italy.
E-mail address: enrico.ammirati@ospedaleniguarda.it (E. Ammirati).
@AmmiratiEnrico (E. Ammirati)