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# Special Issue on ischemic heart disease

## Patrizio Lancellotti, Hélène Petitjean, Alain Nchimi & Bernard Cosyns

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#### **EDITORIAL**

# Special Issue on ischemic heart disease

This issue of Acta Cardiologica is devoted to ischaemic heart disease (IHD). Cardiovascular disease (CVD), primarily IHD, itself usually referring to coronary artery disease (CAD), is the leading cause of death and a major contributor to chronic disease in Western countries [1]. The development of CVD is driven by the complex interplay of genetics, environment (risk factors) and lifestyle. However, cardiovascular risk assessment using established risk scores such as ESC SCORE2 does not place sufficient emphasis on the role of genetic factors [2]. In their study, Krohn et al. have shown that commercially available tests for genetic polymorphisms may provide valuable information about individual genetic cardiovascular risk, potentially guiding future primary and/or secondary preventative therapies for CAD (Figure 1).

Chronic inflammation is recognised as a contributing factor to the development, progression and complications of atherosclerosis. The inflammatory nature of atherosclerosis has been proven by the presence of inflammatory cells, cytokines and chemokines at all stages of the disease. In their study, Soflaei et al. examined the impact of treatment on inflammatory biomarkers in patients with CAD. They showed that the level of highly sensitive C-Reactive Protein (hs-CRP) 1-year after stent implantation decreased despite significantly higher serum levels of pro- and anti-inflammatory cytokines and growth factors [3]. Neutrophils are highly plastic cells that can display heterogeneous phenotypes. Low-density neutrophils (LDNs) are thought to represent an immature, hyperactivated subtype of neutrophils. An increase in LDNs have been found in patients with acute coronary syndrome (ACS) [4]. In their study, Yiu et al. reported a higher frequency of immature LDNs in patients with myocardial infarction compared to healthy subjects [5]. Large prospective studies in patients with type 2 diabetes mellitus have demonstrated that metformin treatment improves cardiovascular prognosis, independent of glycemic control [6]. Cell death is suggested to be a hallmark of cardiac pathology in myocardial infarction and diabetes. The Adenosine MonoPhosphate (AMP)-activated protein kinase (AMPK)/mammalian target of rapamycin (mTOR) signalling pathways play a major role in cell survival/death regulation [7]. Metformin is known to act on AMPK/mTOR pathways. In their diabetic rat model, Zhang et al. showed that metformin can activate autophagic function and decrease infarct size in diabetes-induced ischaemia-reperfusion injury [8]. Cardiovascular complications from cancer therapy have become a leading cause of morbidity and mortality in cancer survivors [9]. Screening for cardiovascular risk factors and anti-cancerrelated complications by dedicated care providers has thus been advocated. In an elegant review, Madias pointed out the higher incidence of CAD in patients undergoing left versus right chest radiation for breast cancer, and that cardiologists and oncologists should be routinely involved in evaluating these patients before treatment and during subsequent follow-up [9].

Imaging plays a key role in the assessment of IHD. Multiple non-invasive cardiac imaging modalities can anatomically delineate or functionally assess for significant CAD, as well as detect the presence of myocardial infarction (MI). In very interesting cases, Sánchez et al. showed that 3D transthoracic echocardiography can be useful in imaging the origin and trajectory of coronary artery, adding valuable data to the 2D image with a single acquisition [10,11]. Cardiac Computed Tomographic Angiography (CCTA) can detect coronary plaque with high resolution, estimate the degree of functional stenosis and characterise plaque features. However, the quality of the imaging and the optimisation of the reconstruction phases can be hampered by the irregularity of the rhythm and an excessively high heart rate. Using a new subtraction method, Zhou et al. showed better accuracy in detecting CAD independent of baseline heart rate, which could expand clinical availability of the technique for patients with elevated heart rate [12]. 2D speckle-tracking echocardiography represents an advanced imaging technique that allows the analysis of global and regional myocardial function [13]. In In their study of 100 patients with ACS, Abdel Mawla et al. showed that global longitudinal strain had a higher diagnostic accuracy for the detection of the severity of CAD than conventional wall motion analysis [14].

Management of CAD is now better guided by the physiological significance of coronary artery stenosis, which can be assessed during invasive coronary angiography by measuring Fractional Flow Reserve (FFR) during adenosine-induced hyperaemia [15]. Quantitative Flow Ratio (QFR) has emerged as a novel angiography-based physiological index for fast computation of FFR without the use of a pressure wire or induction of hyperaemia [16]. Kasinadhuni et al. reported that QFR has a good diagnostic performance in comparison to the gold standard FFR for physiological assessment of intermediate coronary lesions (Figure 2) [17].

Coronary artery Spasm (CAS) is one of the main causes of Ischaemia with No Obstructed Coronary Arteries (INOCA). The diagnosis of CAS usually depends on

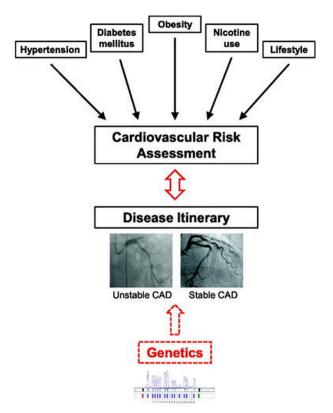


Figure 1. Genetics in CVD (Krohn et al. [2]).

intracoronary drug provocation test, which may cause serious complications (bradycardia, ventricular tachycardia, cardiac shock, ventricular fibrillation, acute myocardial infarction and even death). Wu et al. investigated the accuracy and safety of radial artery provocation tests using ergonovine and acetylcholine in the diagnosis of CAS. The radial acetylcholine provocation test had no diagnostic value for CAS. On the contrary, the radial 160 µg-ergonovine provocation test had good accuracy for CAS diagnosis [18].

Percutaneous Coronary Intervention (PCI) has become a cornerstone in the treatment of patients with CAD, presenting with acute and chronic coronary syndromes. The conventional radial approach has become the access route of choice for performing diagnostic or therapeutic coronary angiography. It has taken precedence over the femoral approach, which is subject to a higher rate of vascular and haemorrhagic complications. The distal radial approach (dTRA) is currently considered a further refinement of the conventional radial approach. It offers the advantage of potentially reducing local vascular complications (spasm, thrombosis of the radial artery). In a prospective observational registry, Escutia-Cuevas et al. evaluated the real-world feasibility and safety of dTRA as the default access site for routine coronary angiography and PCI in a Latin-American centre. The authors confirmed that the success and complication rates of dTRA support its routine use in selected patients [19]. During PCI, the incidence of so-called "uncrossable lesions" is estimated at 2-10% of lesions. Multiple balloons have thus been designed to overcome this problem. The Blimp balloon has a very low scoring profile (0.6 mm) with a very high rated burst pressure (30 atmospheres). In their prospective multicenter randomised controlled trial, Dens et al. showed that the Blimp balloon catheter had no superiority to customary low-profile balloons in uncrossable lesions [20]. Complete revascularization (CR) in ST-segment elevation myocardial infarction (STEMI) patients is currently advocated because it reduces Major Adverse Cardiovascular Events (MACE). In their study, Almeida et al. confirmed in a large Portuguese cohort of STEMI patients with multivessel disease that CR substantially reduced in-hospital and 1-year all-cause mortality and MACE [21]. Left ventricular enlargement/remodelling and the development of chronic heart failure are potent predictors of survival in patients after myocardial infarction [1]. The level of vitamin D is known to modulate the activity of the renin-angiotensin-aldosterone system pathway which modulates the left ventricular remodelling process. In their study, Javadzadegan et al. showed that extremely low levels of vitamin D (<7.5 ng/dL) caused a fivefold decrease in the likelihood of ST-segment resolution after primary PCI in STEMI patients [22]. In his elegant editorial comment, Claeys suggested to correct Vitamin D deficiency in our population in view of its beneficial effect on non-cardiac systems such as the bone formation [1]. Elevated resting heart rate (HR) is associated with worse outcomes in various CV disease [23]. In patients with ACS, Yuksek et al. reported that increased heart rate at discharge was an independent predictor of 1-month mortality. It should be noted that this relationship disappeared after 1-month through 1year follow-up [24]. In STEMI patients managed with primary PCI, a co-existing non-infarct related artery chronic total occlusion (CTO) had an independent association with the evolution of contrast-associated nephropathy [25]. Left ventricular apical thrombus (LVAT) is not a rare complication after anterior STEMI, ranging from 4 to 8% [26]. Bayam et al. evaluated the usefulness of CHA<sub>2</sub>DS<sub>2</sub>VASc Score evaluation to predict the presence of LVAT after myocardial infarction. After analysis of 378 patients presenting with anterior STEMI, it appeared that CHA2DS2VASc Score was an independent predictor for LVAT formation, as well as low left ventricular ejection fraction and left ventricular apical akinesis or aneurysm [27]. Dolu et al. investigated the association between intracoronary thrombus burden and Systemic Immune-Inflammation index (SII) in 425 patients with STEMI. As a result of their analysis, SII emerged as an independent predictor of high thrombus burden in patients with STEMI. The predictor capacity of SII was superior to Neutrophil-Lymphocyte Ratio (NLR), and the Platelet-Lymphocyte Ratio (PLR) [28]. The paper was commented by Pirlet [29]. The impact of intravascular ultrasound (IVUS) on stenting pattern during primary PCI for STEMI was reported in 62 patients. In that study, there was

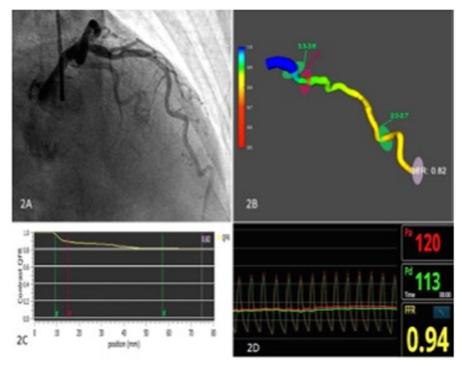


Figure 2. Angiographic image of a tortuous left anterior descending artery showing proximal moderate stenosis (A). The 3D Quantitative Coronary Angiography (QCA) reconstruction of the artery showing stenosis with a minimal luminal diameter (MLD) of 1.7 mm (B). A concordant but different QFR (C) and FFR values >0.80 (D), deferring intervention (Kasinadhuni et al. [17]).

significant difference between IVUS derived and angiographically assessed culprit vessel metrics in patients undergoing primary PCI. Clinical outcomes of this discrepancy need further studies [30].

#### **Disclosure statement**

No potential conflict of interest was reported by the author(s).

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#### Patrizio Lancellotti

Department of Cardiology, CHU SartTilman, University of Liège Hospital, GIGA Cardiovascular Sciences, Liège, Belgium

### Hélène Petitjean

Department of Cardiology, CHU SartTilman, University of Liège Hospital, GIGA Cardiovascular Sciences, Liège, Belgium

#### Alain Nchimi

Department of Cardiology, CHU SartTilman, University of Liège Hospital, GIGA Cardiovascular Sciences, Liège, Belaium

> Department of Radiology, Centre Hospitalier de Luxembourg, Luxemburg, Luxemburg

## Bernard Cosyns

Centrum Voor Harten Vaatziekten (CHVZ), Vrije Universiteit Brussel (VUB), Universitair Ziekenhuis Brussel (UZ Brussel), Brussels, Belgium

In vivo Cellular and Molecular Imaging (ICMI) Center, Vrije Universiteit Brussel (VUB), Brussels, Belgium

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