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Editorial

Highlights from the International Journal of Cardiology Heart & Vasculature: Heart failure, atrial fibrillation, coronary artery disease and myocardial infarction

The field of cardiovascular medicine is highly dynamic, combining scientific opportunities, clinical needs and societal demands with disruptive technological advances, with the ultimate goal to improve global health and make it accessible world-wide. In July 2017, a new editorial board led by the editor-in-chief, Prof. Dobromir Dobrev from Essen (Germany), took over the International Journal of Cardiology Heart & Vasculature. According to the broad scope of this journal we publish papers covering almost all areas of cardiology and vascular medicine including sport, rehabilitation and mental health. After 2.5 years in service we believe that it is time to reflect on our work by highlighting papers focusing on heart failure (HF), atrial fibrillation (AF), coronary artery disease (CAD), and myocardial infarction (MI), which represent some of the journal's main publishing areas.

1. Heart failure

The end of the cardiovascular continuum in patients with cardiovascular risk factors is HF. Despite the growing number of studies with real-world data on HF [1], prediction and optimal management of HF remain challenging. Following HF onset, patients experience a striking deterioration in their clinical course due to cardiac remodeling, leading to pump failure and arrhythmogenesis [2,3]. Although the prognosis of HF patients, notably in those patients with reduced ejection fraction, has improved over the years, likely as a result of improved pharmacological therapy limiting structural remodeling [4], current HF therapy remains suboptimal especially during the "vulnerable period" of hospital discharge. Identifying high-risk patients in HF cohorts is of clinical importance to reduce repeated hospitalizations and to predict patients with higher risk of early mortality [5]. Costa et al. evaluated frailty in HF patients using the Clinical Frailty Scale and established a significant association with 1-year mortality [6]. These simple bed-side scales to assess frailty may provide additional significant prognostic information in acute HF patients.

Pharmacological treatment represents the cornerstone of HF management. Interestingly, HF and diabetes share pathophysiological links; diabetes is present in 35–45% of patients with chronic HF and mortality is doubled in patients with diabetes and HF. Several new targets and treatment strategies have been introduced and discussed during the last years. After years of disappointing studies showing no reduction of cardiovascular events with strict glycaemic control ("glycocentric hypothesis"), some of the novel glucose-lowering drugs (e.g. GLP1 agonists: liraglutide, semaglutide, and SGLT2 inhibitors: empagliflozin and canagliflozin) seem to offer a better control of atherosclerotic burden (GLP1 and SGLT2) and improved HF outcome (SGLT2i) have been shown to prevent HF and renal dysfunction and improve cardiovascular and total mortality [7]. Maranta et al. summarize in their review why the interdisciplinary crosstalk between Cardiologists and Diabetologists is of paramount importance to fully exploit the power of these new pharmacological strategies to select the best therapy for patients with both disorders [8].

In addition to HF with reduced and preserved ejection fraction (HFrEF or HFpEF), HF with mid-range ejection fraction (HFmrEF) has recently emerged as a potential phenotype of HF patients. Webb et al. discuss whether HFmrEF is a distinct clinical entity or an overlap group [9]. They show that HFmrEF patients had the best outcomes, compared to high rates of mortality seen in patients with HFrEF and high rates of heart failure readmissions seen in patients with HFpEF. Only 1/3 of HFmrEF patients transitioned during follow up, with the lowest mortality seen in patients transitioning to HFpEF. It appears that prognosis differs between patients with HFpEF, HFrEF and HFmrEF, making it likely that more subgroups of HF patients with distinct prognoses might exist and HF encompass a continuum wide spectrum.

Left ventricular assist device (LVAD) is a consolidated therapeutically option for patients with advanced HFrEF. Morici et al. presented a narrative review on pathophysiologic mechanisms of platelet activation in patients on LVAD support to minimize ischemic events and pump thrombosis or bleeding complications [10].

In addition to pharmacological and device-based treatment, rehabilitation programs play an important role to ensure treatment adherence and education in HF patients. In Vietnam, the Optimize Heart Failure (OHF) Care Program was established to improve outcomes following HF hospitalization by increasing patient awareness and optimizing HF treatment [11]. The program could be successfully implemented in Vietnam and resulted in high usage of guideline-recommended drug therapy. However, the authors identified that although education was delivered, patient knowledge and practice could be further improved at 6 months after discharge.

Besides the development of rehabilitation programs, the implementation of such programs in daily clinical practice is critically

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important. A pilot study by Balakumaran et al. showed that a nurse-guided medical therapy titration program successfully increased the number of patients in whom pharmacological medication was up-titrated in a timely fashion, which was associated with an enhancement of ejection fraction and a reduction in rehospitalization rates [12]. Nurse-lead programs may be an important and effective alternative to physician-lead programs to implement and monitor guideline-confirm treatment of patients with chronic diseases in an interdisciplinary and integrated care setting [13].

Increased physical fitness through exercise training is an important component of cardiac rehabilitation in patients with chronic diseases. Minotto et al. investigated which factors are associated with patients walking fitness when starting cardiac rehabilitation [14]. In 2047 patients from the National Audit Cardiac Rehabilitation, they found that use of diuretics, socioeconomic status and presence of comorbidities were significant predictors of walking performance in HF patients undergoing cardiac rehabilitation. Identifying reference values and predictors of good response to exercise programs are important steps to design personalized exercise training programs in the future.

2. Atrial fibrillation

AF is the most common sustained arrhythmia and is associated with significant morbidity, increased risk of stroke and thromboembolism, brain damage [15], reduced quality of life, and increased mortality [16–20]. Symptoms in AF patients include palpitations and reduced exercise tolerance, partly due to reduced oxygen uptake and impaired heart rate responses [21–22]. Concomitant risk factors such as hypertension, HF, obesity, metabolic syndrome, sleep apnea and ageing lead to structural remodeling processes in the atria, which contribute to the progressive nature of AF and the reduced efficacy of pharmacological and catheter-based rhythm-control strategies [19,23,24]. Fibrosis is a prominent feature of atrial remodeling, with epicardial fat tissue importantly contributing to the arrhythmogenic fibrotic substrate, thereby promoting the recurrence of AF in patients undergoing ablation procedures [25]. AF is increasingly considered the consequence of distinct types of atrial cardiomyopathy [26].

The arrhythmogenic consequences of risk factors depend on and interact with the concomitant clinical conditions. One example is AF associated with endurance sports. Ayinde et al. systematically evaluated and summarized all published observational data on the association between competitive sports and AF [17]. Age appears to modify the risk of AF in athletes, which also suggest, that long-term exposure to (sub-) clinical risk factors in athletes may contribute to AF, particularly with advanced age.

Anticoagulation in AF patients is crucial to prevent stroke [16]. Although the use of anticoagulants is relatively satisfactory in the industrialized world, a large proportion of AF patients with concomitant stroke risk factors do not take anticoagulants in several parts of the world. Tegene et al. demonstrated in a community-based cross-sectional study in Ethiopia that the prevalence of AF is 4.3% and thus higher than in many other countries, with common risk factors being sex, current smoking, hypertension, and higher body mass index in this cohort [27]. More than two-third of study participants with AF had a guideline-based indication for oral anticoagulants [28].

Currently, an ECG-recording of the arrhythmia is needed for the diagnosis of AF. New ECG algorithms try to identify patients at high risk of developing AF by detecting precursors in the ECG during sinus rhythm. Im et al. showed that a higher atrial premature contraction (APC) burden, higher fastest APCs running heart rate and lower minimal heart rate were associated with new-onset AF in asymptomatic patients with APCs in the long-term follow up [29]. Early detection of ECG-derived AF precursors may be useful to identify patients in whom a more intense AF screening should be performed to document the arrhythmia and initiate appropriate treatment.

In addition to pharmacological approaches to maintain sinus rhythm and prevent AF recurrence [18], different catheter-based ablation techniques exist to achieve pulmonary vein (PV) isolation. In addition to radiofrequency ablation, which has proven to be safe [30], cryo-balloon techniques have been introduced as a comparable and equally effective approach, particularly in patients with paroxysmal AF. Until now, the success in PV isolation during cryo-balloon ablation is monitored by real-time recordings of PV electrograms. Pott et al. demonstrated that the interpretation and real-time observation of PV electrograms during cryo-ablation is more valid in sinus rhythm than in AF [31]. Therefore, electrical cardioversion at the beginning of the procedure should be considered. Prochnau et al. evaluated a purely temperature-guided approach of cryo-balloon ablation completely without visualization of real-time recordings [32]. They discovered that temperature-guided cryo-ablation without real-time recordings is feasible and safe without reducing efficacy, if a newer second-generation cryo-balloon is used. Deep nadir temperatures are necessary for long term-success. This and other studies may further simplify catheter-based PV isolation approaches, which may make this technique more widely usable. In addition to catheter-based strategies, concomitant maze IV surgery is still used to maintain sinus rhythm in patients undergoing open heart surgery. However, concomitant maze IV surgery provided limited long-term success in obtaining sinus rhythm with no difference in 10-year event-free survival [33].

Hybrid antiarrhythmic therapy combining drugs with devices and interventional therapy enhances the success rate of rhythm control strategies [18,50]. Simon et. al. demonstrated the increased success of electrical cardioversion using pre-medication with vernakalant to facilitate the conversion rate [34]. They proved also the safety of the protocol; however, some patients developed atrial flutter after vernakalant infusion (which converted spontaneously to sinus rhythm in all patients).

3. Coronary artery disease and myocardial infarction

MI with its complications and structural cardiac consequences is one of the main causes of HF and cardiovascular mortality in the Western world. In patients with acute MI, predictors for cardiovascular outcomes and mortality are important for risk stratification and management of patients during the first weeks after the initial event and several studies have assessed the role of clinical risk factors and several biomarkers. Age influences outcome in a more pronounced way in females than in males [35]. Females are likely to exhibit worse overall survival, and older females are at higher risk of HF. Acute HF in patients presenting with acute coronary syndrome is associated with worse prognosis, but its identification is often challenging. Novel biomarkers such as circRNA MICRA may be useful to improve risk stratification after MI [36]. Arrigo et al. showed that plasma adrenomedullin is a marker associated with acute HF severity in patients with acute coronary syndrome [37]. Lipoprotein (a) levels are associated with a higher prevalence of thin-cap fibroatheroma and increased plaque vulnerability in patients with CAD [38]. Severe frailty assessed by a simple questionnaire is associated with mid-term mortality in ST elevation MI patients [39]. Another predictor for outcome after MI is the time of presentation after the index event. Female sex, diabetes, and absence of chest pain are strong predictors of presentation delay, and long-term mortality is significantly increased in those presenting very late [40]. If early percutaneous catheter interventions are not possible, fibrinolysis is commonly used as the first treatment strategy in patients with acute ST-elevation

MI. Mongkhon et al. showed that fibrinolytic injection before referring patients with STEMI to catheter-capable settings has no clinical benefit and even increased the risk of major bleeding [41]. Thus, use of routine fibrinolytic injection in this setting is no longer routinely recommended and should be considered on an individual basis only. It is of prognostic importance how patients present in the hospital. ST-elevation MI complicated by out-of-hospital cardiac arrest remains a high-risk group associated with high in hospital mortality and beyond 30 days the occurrence of cardiac arrest is significant predictor of all-cause and cardiac mortality [42]. In addition to ST-elevation during the ischemic event, bundle branch block morphology of the QRS complex may predict outcomes after MI. Timoteo et al. showed that patients with bundle branch block have worst outcome after an acute coronary syndrome, particularly if they develop a right bundle-branch block [43]. Finally, inducibility of ventricular arrhythmias during invasive electrophysiological studies may be a strong predictor of malignant arrhythmias in a subset of post-MI patients with impaired ejection faction and may be a good criterion in selecting patients who could benefit from ICD implantation [44]. All these factors need proper consideration when trying to identify patients at high risk after MI.

Some patients who present with chest pain may not have CAD but may be symptomatic because of coronary artery spasm or MI with non-obstructive coronary arteries (MINOCA). Identification of these alternative causes for chest pain is difficult in the clinical setting and often requires invasive functional measurements. Lin et al. developed in 976 consecutive patients with acute chest pain a prediction score to identify patients with chest pain due to coronary artery spasm [45]. The score included: angina at rest alone (10 points), positive of hyperventilation test (8 points), allergies (3 points), asthma, ST-segment elevation and myocardial bridge (2 points each). The cut-off baseline value for the clinical diagnostic score system was set to 11–12 points with specificity of 91.0–93.3% and sensitivity of 90.7–92.9%, respectively. This clinical diagnostic score system may help to prescreen for coronary artery spasm in patients with acute chest pain. Additionally, several invasive and non-invasive strategies are currently used to assess the functional significance of coronary lesions [46,47] and coronary CT angiography is a widely used strategy to detect significant coronary lesions non-invasively [48,49].

4. Outlook

HF, AF, CAD and MI are important and prevalent clinical conditions. Despite significant advances, predictive, diagnostic and therapeutic modalities remain suboptimal. The diagnosis, therapy and long-term management of such patients require a multidisciplinary and integrated care model to ensure not just resolution of the initial clinical presentation, but also to allow initiation of individualized and patient-centered approaches to control symptoms and implement secondary prophylaxis programs that improve patient prognosis. We strongly believe that future prospective clinical investigations in these important areas of medicine will further facilitate the development of novel diagnostic and therapeutic approaches and hope that our journal will further serve as a platform to disseminate new clinical knowledge to the community.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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