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January 2015 saw the launch of a new journal in the European Heart Journal family - *European Heart Journal: Cardiovascular Pharmacotherapy*. What were the highlights of cardiovascular pharmacotherapy in 2015? As in every year, there were advances in the field of coronary artery disease, heart failure, atrial fibrillation, antithrombotics and anticoagulation, prevention and more. However, it was in the treatment of diabetes that 2015 saw the first study showing outcome benefit with empagliflozin, a new class of antiglycemic drug [1]. The EMPA-REG outcome trial showed improved survival and less hospitalization for heart failure: it is changing concepts and practice1. The new era of outcome trials follows the acute awareness of the need to examine cardiovascular safety of anti-diabetic drugs [2,3]. Assuming that the findings are a class effect, 2 other ongoing long-term outcome studies examining a SGLT2 inhibitor-based therapeutic regimen vs standard care are attracting widespread attention (DECLARE-TIMI 58 study with dapagliflozin, VERTIS with ertugliflozin) and will provide essential information in this regard. More recently, and most likely by a different mechanism, survival benefit and reduced cardiovascular events were shown in patients receiving the human glucagonlike peptide 1 (GLP-1) analog liraglutide as part of their anti-glycemic management [4].

The new journal published several papers relating to diabetes and its cardiovascular complications. In a sub study from the ARISTOTLE atrial fibrillation trial [5], apixaban had similar benefits in reducing stroke, decreasing mortality and causing less intracranial bleeding than warfarin in patients with and without diabetes [6]. Singh and co-workers reported that despite rapid revascularization and treatment of hyperglycemia in patients with acute myocardial infarction, admission hyperglycemia was associated with an increased mortality [7].

Coronary artery disease and acute coronary syndromes were as always a major focus of attention in 2015. Jørgensen and co-workers reported temporal changes in patient characteristics and pharmacotherapy in 156,496 patients referred for coronary angiography between 2000 and 2009 in Denmark. During a 10-year period, there was an increase in mean age of patients, the proportion of female patients, and a 56% increase in the number of coronary angiographies performed [8]. Another study examined the relation between serum potassium levels and short-term mortality in patients receiving loop diuretics after acute myocardial infarction [9]. Potassium levels outside the 3.9–4.5 mmol/L range, especially hyperkalemia, were associated with a substantially increased risk of death.

Regarding antithrombotic therapy, glycoprotein IIb/IIIa inhibitors reduce myocardial infarction and peri-procedural thrombotic complications in patients undergoing percutaneous coronary intervention. They may cause bleeding and thrombocytopenia, and risk–benefit should be kept in mind [10]. The EYESHOT study assessed antithrombotic therapies in medically managed patients with acute coronary syndromes (ACS) [11].

Almost one-third of EYESHOT ACS patients were managed without revascularization during the index hospitalization. In those treated without revascularization, a lower use of recommended antiplatelet therapy and worse clinical outcome was observed, supporting current guideline management.

The issue of cardioprotection around myocardial reperfusion is still unsettled and the use of catalytic antioxidants could still just possibly find a role [12]. Also not to be neglected is the question of microvascular dysfunction, even though there are few data regarding the effectiveness of pharmacological treatments in these patients [13]. In secondary prevention, poor adherence to ACE-I/ARB prescription medication was associated with a 20% increased risk of recurrent AMI [14]. The Platelet inhibition Registry in ACS EvalUation Study (PIREAUS) is a European initiative of experts in cardiology who are managing national or international acute coronary syndrome registries. About 20 completed or ongoing such registries have been set up to document clinical experience with ACS patients, who undergo percutaneous coronary intervention and who are treated with antithrombotic drugs. PIRAEUS aims to

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expand clinical knowledge on how to provide optimal care and therapy to ACS patients [15].

Atrial fibrillation mandates the optimal use of anticoagulant therapy [16]. Aspirin is now discouraged. In an observational study of 5426 Chinese patients with atrial fibrillation, aspirin was associated with higher risk of gastrointestinal bleeding compared with warfarin and the risk of gastrointestinal hemorrhage in patients on warfarin increased progressively with worsening TTR [17]. While NOACs are now in widespread use [18], the benefit–risk balance may be difficult [19] and the challenge of double or triple antiplateletanticoagulation in patients with AF and ACS and/or undergoing percutaneous coronary intervention not always straightforward [20,21]. Ongoing clinical trials (PIONEER-AF, Re-DUAL PCI, AUGUSTUS) may shed more light on these issues.

Heart failure (HF) remains a major topic in cardiovascular pharmacotherapy. Optimized pharmacotherapy is a mainstay of heart failure management and adherence to guidelines portends survival benefit [22], including in patients who have undergone cardiac resynchronization therapy device implantation [23]. Although optimal hemoglobin level for the HF patient is still debated, as is the role of erythropoetic stimulating drugs, iron replacement in patients with HF with reduced ejection fraction has been shown to improve symptoms and exercise capacity [24].

Valsartan/sacubitril (LCZ696) is a first-in-class angiotensin receptor neprilysin inhibitor (ARNI) which has been shown to enhance the endogenous natriuretic peptide actions on neurohormonal activation. The clinical benefit in HF patients was demonstrated in the PARADIGM trial [25]. LCZ696 was also effective in reducing blood pressure in several small studies; its effectiveness and safety in the management of hypertension remain to be proven in larger patient populations [26]. The treatment of hypertension reopened to major discussion following the dubious role of renal denervation and the findings of the only randomized trial (Symplicity HTN-3) [27].

What other topics were published in *European Heart Journal: Cardiovascular Pharmacotherapy* in its first year? A review paper discussed cardiorenal protection during chronic renin–angiotensin–aldosterone system suppression [28]. Use of NSAIDs had an increased risk of atrial fibrillation in patients with prior myocardial infarction [29]. Colchicine had superior clinical efficacy compared with standard therapy for the prevention of recurrent pericarditis and post-pericardiotomy syndrome [30]. The pharmacological challenges in the management of patients with concomitant cardiovascular and chronic obstructive pulmonary disease were reviewed by Ceconi and his group [31].

In 2016, the ***European Heart Journal: Cardiovascular Pharmacotherapy*** (EHJ-CVP) was accepted for inclusion in Medline, giving rise to unrestricted and retro-active MEDLINE referencing critical to academic publishing. Achieving such an accomplishment by the date of June 23, 2016 implies that this journal has been on the publishing arena less than 18 months before reaching this milestone. In the history of PUBMED, this represents an unprecedentedly short time-span.

What were the articles representing the evident quality of the EHJ-CVP during the first months of 2016? The major topics in cardiovascular medicine were addressed:

Cardiovascular Pharmacotherapy. An important position paper by the working group for Cardiovascular Pharmacotherapy of the ESC was published in the EHJ-CVP. In this comprehensive work, the authors shed light on what is known about the cardiovascular safety of non-steroidal anti-inflammatory drugs [32]. These drugs deserve close attention in patients, given their well-documented side effects such as elevated blood pressure (BP). Likewise, a review by Kumar et al. elaborates on the cardiovascular safety of anti-diabetic drugs [33]. This aspect is translated even further by the assessment of cardiovascular risk of *new* drugs used in diabetic patients, given by Zannad and associates [34].

Arrhythmia. In a paper from Johnson et al., studying a cohort of 5633 men, a direct relationship of individual BP levels, and the risk of developing atrial fibrillation (AF) was revealed [35]. Another insightful paper was published by C Hayward, describing the trends in Great Britain of prescribing oral anti-arrhythmic drugs during a 16-year period [36]. Two drugs, amiodarone and sotalol, were prescribed less often over time, while flecainide showed an increase in prescriptions. These observations are useful when deciding between rate-control versus rhythm-control strategies. Elaborating on stroke prevention in AF, Filskov Overvad and co-workers provide new insights into anticoagulation treatment thresholds [37]. The enigma of pharmacological approaches in cardiac arrest is reviewed by Lundin and co-workers [38]. Even without large-scale trials evidence, the clinician here gets clear guidance as to the use of the various therapies in these dramatic clinical situations.

Heart Failure (HF). Although significant improvements in prognosis of HF have been achieved during the last two decades, there is still staggering mortality encountered, particularly in acute HF. Hence the search for new molecules is imperative. One of the promising principles is cenderitide, a dual natriuretic peptide receptor activator which may play a particular role in cardiorenal disease. Dr. Lee et al. explain in their contribution its mechanism of action at the receptor level [39]. At an even later stage of development is serelaxin in the treatment of acute HF, as reviewed by Diez and Ruilope [40]. While new drugs need scrutiny, there is still much to learn about the oldest drug used in HF: digitalis. Erath and co-workers assessed its utility in the particularly sick patient population of ICD-implanted HF patients [41]. Their results did not support the use of digitalis in these patients. Pitt and his group described the current indications and the future prospects of using mineralocorticoid receptors in HF [42]. Finally, an interesting molecule, melatonin, and its multi-organ effects is portrayed in the enlightening overview by Opie [43].

Acute coronary syndromes (ACS) and antithrombotic therapies. Not surprisingly, a major part of the contributions pertain to coronary heart disease (CHD), its pathophysiology and its therapies. An important review article by P. Widimsky provides the readership with a state-of-the-art listing of current antithrombotic regimens used during interventions for a wide variety of conditions, including myocardial infarction, stroke, and arrhythmias [44]. Also Serebruany et al. focus on the related topic of dual antiplatelet therapy, with an emphasis on renal impairment, a known factor of increased bleeding risk [45]. Based on their experiments it is shown that platelet reactivity is altered in patients with renal dysfunction. A different aspect is evidence gained from registries, such as the one given by Danchin and co-workers in their article on patients post STEMI [46]. Their research shows that mortality, ischemic events and bleeding complications occur less often than what could be expected based on the corresponding phase-II trials of antithrombotic drugs. These findings are interesting in light of the publication by Sahlén et al., who showed that the use of Ticagrelor in Sweden was preferentially used in patients at low risk after an ACS [47]. Finally, a recurrent debate regarding proton-inhibitors and their concomitant use with platelet inhibitors is put to rest in a paper by Fortuna and co-workers: there was no increased risk of cardiovascular events in this co-prescription setting in patients with CHD [48]. Finally, a novel approach is described in an article by Manzo-Silberman, focusing on desensitization and basophil activation in patients who have documented aspirin hypersensitivity [49].

Also pathophysiology was covered in the EHJ-CVP: the modality of attempting functional modifications of T-cells to prevent atherosclerosis has been the topic of an important review article [50]. Finally, given the increasing role of biomarkers in a variety of cardiovascular diseases, one review article sheds light on the biomarker D-dimer, and elaborates on its clinical importance in diagnostication and prognostication [51].

Risk factors. One major risk factor for CHD is diabetes. The emerging role of gliptins is meticulously reviewed in an article by Brenner [52]. In light of the role of lipids in the pathophysiology of CHD, two articles deal with this particular risk factor: Navarese and co-workers discuss the clinical implications of PCSK9 inhibition, attracting growing interest in preventive cardiology [53]. Further, Kallend and associates demonstrate