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EDITORIAL

Global Cardiology issue highlights

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Welcome to the June issue of *Global Cardiology*, a journal devoted to the dissemination of knowledge, impact and research of relevance to cardiovascular physicians and healthcare professionals worldwide. True to this purpose, we are pleased to introduce diverse and stimulating contributions and comments.

As benefits our *global* title and nature, we commence this issue with two reports from the Middle East and Africa. The first is a fascinating bibliometric analysis of cardiovascular (CV) research in the Arab World.[1] This growing powerhouse applies first world medicine to a growing population with modern emerging issues overlaid on historical discase burdens. The increasing wealth of the region has altered lifestyles and body weight in equal measure and created a big migrant influx that has affected indigenous disease patterns as we see a substantial growth in CV disease burden but also pleasingly a significant expansion of quality CV research output emanating from this region, with Qatar and Lebanon having the highest ratio of CV publications and Qatar the highest number per million populations and Tunisia the most in absolute terms. We continue to support this growing powerhouse region that has so much to offer the world, as we adapt to the rapid *Westernisation* of chronic disease burdens of diabetes, obesity and related CV disorders. There is also an original report of relevance to the Middle East and much of North Africa and that is the effect of Ramadan related fasting on CV disease patients from Refaat of American University of Beirut, showing reassuringly no significant difference between Ramadan and non-Ramadan months regarding the incidence of cardiovascular events (stroke, myocardial infarction, unstable angina, atrial fibrillation, heart failure), although isolated examples show certain complications could be triggered by the post-fast larger meals.[2]

Another paper is from the talented team of Karaye *et al.*, who examined the epidemiology of peripartum cardiomyopathy in Nigeria. Maternal health is an ongoing problem throughout Africa and there is a high rate of multiple pregnancies occurring naturally. What has more recently become evident is there is an increased risk of peripartum cardiomyopathy (PPCM). Comprehensive population surveys are however lacking. This hospital survey from Nigeria follows reported incidence rates as high as 1:100 deliveries in Nigeria representing up to 52% of all cardiomyopathies in selected hospital series, although there does appear to be wide variability between African Countries, and within the countries, being more common among the poorer rural populations. Clinical outcomes are much worse in Africa than in Western Europe and North America with mortality rates as high as 24.2% at 6 months and 47.4% at 1 year of follow-up having been recorded in Kano, Nigeria, and similar rates in Burkina Faso, and slightly lower rates in Zimbabwe and in South Africa. The ongoing peripartum cardiomyopathy in Nigeria (PEACE) Registry and the worldwide EURObservational Research Programme (EORP) on PPCM will hopefully shed more light on the epidemiology of PPCM in Africa.[3] A report from that registry is also presented in this issue investigating the issue of selenium deficiency in a prospective longitudinal study of 108 apparently healthy pregnant women.[4] During pregnancy, 6 subjects (5.6%) and 20 subjects (18.5%) had left ventricular (LV) systolic and diastolic dysfunction; after delivery, 9 subjects (10.2%) (p=0.340) and 14 subjects (15.9%) (p=0.631) had LV systolic and diastolic dysfunction. However, only 2.8% of the subjects had selenium deficiency (<70 µg/L), and serum selenium did not significantly correlate with indices for LV systolic or diastolic dysfunction.

Another study included in the issue is from a *stellar* group of international investigators led by Stephan von Bardeleben, who reports the baseline echocardiographic data of the third large Mitraclip study for secondary MR, RESHAPE-HF-2 which is expected to be published in the next few months.[5] Importantly, it compares these to the two previous Mitraclip studies which had dramatically different results, COAPT and Mitra-FR. In the 505 patients randomized in RESHAPE-HF-2 [mean age 70 years, 20% female, mean LV ejection fraction (LVEF) 31%] the mean regurgitant volume was 37±12 mL, while mean proximal iso-velocity surface area (PISA) radius was 0.72 cm and less than half of the patients (44%) had mitral regurgitation (MR) severity grade 4+. The mean effective regurgitant orifice area (EROA) among patients in RESHAPE-HF2 (0.25 cm^2) was lower compared to patients in either MITRA-FR (0.31 cm^2) or COAPT (0.40 cm^2) trials. Regurgitant volumes in RESHAPE-HF2 were between those of

MITRA-FR (45 mL) and COAPT (27 mL) as were LV end-diastolic volumes, despite similar LVEF values. The authors conclude that RESHAPE-HF2 patients were characterized by moderate-to-severe FMR, with a smaller PISA radius, and fewer MR severity grade of 4+, lower mean EROAs and regurgitant volumes compared to previous trials. Thus, RESHAPE-HF2 is targeting a distinct cohort of patients who have less severe FMR compared to patients in COAPT trial, but have high left atrial volumes. We await the final results eagerly.

Anker *et al.* have published an authoritative review of how we should measure and interpret multiple clinical trial end-points, with a focus on recent heart failure trials where such end-points are really being promoted and accepted.[6] The expense of modern trials makes it imperative to attempt to gather as much clinical information as we can from such cost and patient effort; hence, we need strategies to obtain these data avoiding unreliable chance findings. Such procedures to prevent over-frequent statistical testing will require us to get more familiar with modern techniques such as the Bonferroni, Holm and Hochberg test procedures. Therefore, I recommend reading this article carefully and practicing it in academic journal clubs, since clinical trial methodology is unquestionably something that modern cardiology trainees require to keep abreast of to understand and interpret developments in their chosen field.

Additionally, some colleagues (including the international leader Javed Butler *et al.*) have produced a topical and timely meta-analysis and systematic review on the effects of SGLT2 inhibitors on health status in heart failure.[7] They reviewed quality of life (QoL) data mainly based around the KCCQ results and related this to the effects of SGLT2i's across the spectrum of LVEF. They included 12 trials with over 23,000 patients and showed that SGLT2i significantly improved QoL at 12-16 weeks, 32 weeks and 52 weeks of therapy. Results were similar between patients with heart failure with reduced ejection fraction (HFrEF) or heart failure with preserved ejection fraction (HFpEF), acute/worsening or chronic HF, and irrespective of which SGLT2i was trialed, adding QoL improvement as a hallmark feature of HF therapy with an SGLT2 inhibitor. Treatment for obesity-related HFpEF is also a hot topic. A thorough, anonymous, US population-based online survey with 200 medical professionals was completed by 114 patients who self-reported having HFpEF.[8] Findings included the fact that half of these patients waited an average of 22 months for their HFpEF diagnosis, which came mostly from a cardiologist. The treatments most recommended by cardiologists for the ongoing treatment of HFpEF included lifestyle changes (91%), diuretics (87%), beta blockers (76%), and angiotensin-converting enzyme inhibitors (71%). Heart failure specialists (29%) were more likely than general cardiology specialists (12%) to recommend prescription weight-loss medications for management of HFpEF, although few reported having received formal training in obesity management, something that will nearly need correction in future years.

A paper from Bari (Italy) looked at Galectin-3 (Gal-3) overexpression and its possible role in increasing cardiac fibrosis and remodeling in LV hypertrophy.[9] The authors reported on 19 surgical specimens taken from the interventricular septum of 8 patients with Tetralogy of Fallot, 4 patients with aortic valve stenosis, 1 cardiac explant affected by dilated cardiomyopathy, and 6 myocardial biopsies of patients waiting for heart transplantation.
Cytoplasmic expression of Gal-3 was seen in the 4 patients with aortic valve stenosis (diffuse in 3 and mild in 1), in the 1 patient with cardiac explant (mild) and in the 4/6 transplanted hearts (mild and focal in 3 and diffuse in 1). The 8 patients affected by Tetralogy of Fallot and 2 patients with transplanted hearts did not show this feature however, leading the authors to conclude that Gal-3 may play a role only in specific forms of cardiac hypertrophy.

Last but not least, the Gottingen cardiology group reported on the impact of iron deficiency (ID) on exercise intolerance and depressive symptoms in patients with asymptomatic chronic systolic heart failure, showing that ID is common even in asymptomatic HFrEF patients. In a multivariable model, ID predicted both a lower breathing efficiency and a worse NYHA status, making a call for further evaluation in this patient cohort.[10]

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