1. **Dronedaron in high-risk permanent atrial fibrillation.** Connolly SJ, Camm AJ, Halperin JL, et al, PALLAS Investigators. *N Engl J Med* 2011;365:2268–76. doi: 10.1016/S0019-4832(12)60031-5

Dronedaron is a new anti-arrhythmic drug developed for the management of atrial fibrillation (AF) and in major trials like Euridis/Adonis and Athena has been shown to reduce AF recurrence, slow the ventricular rate and reduce cardiovascular outcomes and deaths in patients with paroxysmal and persistent AF. In the background of these studies, PALLAS trial was designed with the hypothesis that patients with high-risk permanent AF would similarly benefit from dronedaron. This trial included patients aged ≥ 65 years with permanent AF of ≥ 6 months duration and at least one risk factor. Patients were randomised to receive dronedaron (400 mg twice daily) or placebo and both the groups were well matched with clinical characteristics and risk factors which included coronary artery disease (CAD) (40.8% vs 41.2%), previous stroke or transient ischaemic attack (26.9% vs 28.3%), symptomatic heart failure (14.4% vs 14.8%), a left ventricular ejection fraction of 40% or less (21.3% vs 20.7%), peripheral arterial disease (PAD) (11.6% vs 13.2%); or the combination of an age of ≥ 75 years, hypertension, and diabetes (18.2% vs 17.1%). CHADS₂ score of ≥ 2 was seen in 88.1% in the drug arm and 89.3% in the placebo arm. The first co primary outcome was stroke, myocardial infarction, systemic embolism, or death from cardiovascular causes. The second co primary outcome was unplanned hospitalisation for a cardiovascular cause or death. The trial was prematurely terminated for safety reasons after a year of enrolment when 3236 patients had undergone randomisation. The first co primary outcome occurred in 43 patients receiving dronedaron and 19 receiving placebo (hazard ratio, 2.29; 95% confidence interval [CI], 1.34–3.94; $P=0.002$). There were 21 deaths from cardiovascular causes in the dronedaron group and 10 in the placebo group (hazard ratio, 2.11; 95% CI, 1.00–4.49; $P=0.046$), including death from arrhythmia in 13 patients and 4 patients, respectively (hazard ratio, 3.26; 95% CI, 1.06–10.00; $P=0.03$). Stroke occurred in 23 patients in the dronedaron group and 10 in the placebo group (hazard ratio, 2.32; 95% CI, 1.11–4.88; $P=0.02$). Hospitalisation for heart failure occurred in 43 patients in the dronedaron group and 24 in the placebo group (hazard ratio, 1.81; 95% CI, 1.10–2.99; $P=0.02$). The occurrence of co primary end point doubled in the dronedaron arm predominantly due to increase in rates of stroke and death from cardiovascular causes. ANDROMEDA trial had earlier shown increased cardiovascular mortality with this drug in patients with severe LV systolic dysfunction. PALLAS reproduced this trend and conclusively showed that dronedaron increased rates of heart failure, stroke, and death from cardiovascular causes in permanent AF patients with high-risk for major vascular events and should not be used in this group of patients.

2. **Prevention of ventricular fibrillation episodes in Brugada syndrome by catheter ablation over the anterior right ventricular outflow tract epicardium.** Nademanee K, Veerakul G, Chandanamattha P, et al. *Circulation* 2011;123:1270–9. doi: 10.1016/S0019-4832(12)60032-7

Brugada syndrome is an autosomally transmitted channelopathy and one of the important causes of sudden death in the young with apparently normal hearts. The electrophysiological mechanisms resulting in the abnormal electrocardiogram (ECG) pattern in this syndrome are unclear. Implantable cardioverter defibrillator (ICD) is the only effective treatment to prevent sudden death in these patients but is difficult solution in the very young, in low-income communities and in those with frequent ventricular fibrillation (VF) episodes necessitating frequent ICD discharges. Haissaguerre et al. earlier showed the efficacy of radiofrequency ablation in these patients by targeting PVC's originating from right ventricular outflow tract (RVOT). This paper describes endocardial and epicardial electroanatomic mapping in 9 patients with type I Brugada syndrome having recurrent VF episodes necessitating ICD discharges. It demonstrates the presence of abnormal arrhythmogenic substrate exclusively in the anterior RVOT epicardium in the form of low amplitude (<1 mv) fractionated electrograms (>130 ms duration) and polyphasic late potentials (>100 ms) after QRS complex on surface ECG) which cause delayed depolarization to cause arrhythmias. Such abnormal electrograms were not seen in the endocardial surface of the same region of RVOT. Ablation at these epicardial sites rendered ventricular tachycardia (VT)/VF non-inducible (7 of 9 patients [78%]; 95% confidence interval [CI], 0.40–0.97, $P=0.015$) and normalisation of the Brugada ECG pattern in 89% (95% CI, 0.52–0.99; $P=0.008$). Long-term follow-up (20 ± 6 months) showed no recurrent VT/VF in all patients off medication (except 1 patient on amiodarone). This paper effectively proves the existence of a localised electrical substrate in patients with Brugada syndrome and presents the potential feasibility of radiofrequency ablation in these patients having recurrent ICD shocks or storms of ventricular arrhythmias.

3. **Endocardial radiofrequency ablation for hypertrophic obstructive cardiomyopathy acute results and 6 months' follow-up in 19 patients.** Lawrenz T, Borchert B, Leuner C, et al. *J Am Coll Cardiol* 2011;57:572–6. doi: 10.1016/S0019-4832(12)60033-9

Endocardial radiofrequency (RF) ablation of septal hypertrophy (ERASH) is a new approach to reduce left ventricular outflow tract (LVOT) gradient in hypertrophic obstructive cardiomyopathy (HOCM) by inducing a discrete septal contraction disorder. The purpose of this study was to study the safety and efficacy of this procedure for LVOT gradient reduction in HOCM. Nineteen severely symptomatic patients despite medications with LVOT gradients of ≥ 50 mmHg at rest or after provocation were enrolled.

The mean age was 60.7 ± 12 years. In 8 patients previous transcatheter ablation of septal hypertrophy (TASH) had been ineffective. The RF energy was delivered to the most proximal parts of the septum in the immediate vicinity of LVOT. A region of 2 cm was ablated with a therapeutic end point of achieving a gradient of <50 mmHg. In 9 patients, the left ventricular septum was ablated, and in 10 patients, the right ventricular septum was ablated. Follow-up examinations (echocardiography, 6-minute walk test, bicycle ergometry) were performed 3 days and 6 months after ERASH. The procedure resulted in reduction of 62% in resting gradients and 60% in provoked gradients. It was associated with improvement in New York Heart Association (NYHA) class (from 3.0 ± 0.0 to 1.6 ± 0.7) and 6-minute walk test (from 412.9 ± 129 m to 471.2 ± 139 m) all of which were sustained at 6 months. In this series 21% had atrioventricular (AV) block requiring permanent pacemaker implantation and 1 patient had cardiac tamponade. It is possible that conduction system damage could have resulted from deep lesions caused by high RF energy (40–70 W), delivered by irrigated tip ablation catheter particularly when right ventricular side of the septum was ablated. The ERASH is a promising therapy for obstructive HOCM; however, further refinements in procedure are necessary before this procedure can be offered on a larger scale.

4. Use of secondary prevention drugs for cardiovascular disease in the community in high-income, middle-income, and low-income countries (the PURE Study): a prospective epidemiological survey. Yusuf S, Shofi qul Islam SQ, Chow CK, et al, Prospective Urban Rural Epidemiology (PURE) Study Investigators. *Lancet* 2011;378:1231–43. doi: 10.1016/S0019-4832(12)60034-0

A large burden of cardiovascular disease exists in the low-income and middle-income countries, however the use of proven medications for secondary prevention these countries is unknown. Prospective Urban Rural Epidemiology (PURE) study was designed to study the use of proven effective secondary prevention drugs (antiplatelet drugs, β -blockers, angiotensin-converting-enzyme [ACE] inhibitors or angiotensin-receptor blockers [ARBs] and statins) in individuals with a history of coronary heart disease (CHD) or stroke. Individuals aged 35–70 years from rural and urban communities from countries of varied economies were recruited. Standardised questionnaires were administered by telephonic or personal interview to collect data on presence of cardiovascular disease and use of proven medications for secondary prevention and anti-hypertensive drugs. Totally 153,996 adults from 628 (348 urban and 280 rural) communities in 17 countries with incomes classified as high (three countries), upper middle (seven), lower middle (three), or low (four) were enrolled between January 2003 and December 2009. Around 5650 participants had a self-reported CHD event (median duration 5 years) and 2292 had stroke (median duration 4 years). Use of medications by patients with cardiovascular disease were antiplatelet drugs (25.3%), β -blockers (17.4%), ACE inhibitors or ARBs (19.5%), or statins (14.6%). Use was highest in high-income countries (antiplatelet drugs 62.0%, β -blockers 40.0%, ACE inhibitors or ARBs 49.8%, and statins 66.5%), lowest in low-income countries (8.8%, 9.7%, 5.2%, and 3.3%, respectively), and decreased in line with reduction of country economic status (P trend <0.0001 for every drug type). Fewest patients received no drugs in high-income countries (11.2%), compared with 45.1% in upper middle-income countries, 69.3% in lower middle-income countries, and 80.2% in low-income countries. Drug use was higher in urban than rural areas (antiplatelet drugs 28.7% urban vs 21.3% rural, β -blockers 23.5% vs 15.6%, ACE inhibitors or ARBs 22.8% vs 15.5%, and statins 19.9% vs 11.6%; all $P < 0.0001$), with greatest variation in poorest countries (P interaction <0.0001) for urban vs rural differences by country economic status). Two-third of the under usage of medications was related to the stage of economic development of the country and 1/3rd to individual factors which included younger people, lower level of education, female gender, smokers, non-hypertensive, non-diabetic, and non-obese individuals. Globally there a significant under usage of medications for secondary prophylaxis and this is more striking in low-income countries. Systematic programmes to ensure increased and appropriate use of proven drugs for secondary prevention are needed in most countries.

Perspective

Our knowledge regarding the usage of medications by patients with CAD or strokes is limited to data available from published clinical trials. This paper is unique in illustrating the real life situation prevalent globally where there is a serious under usage of proven medications including inexpensive drugs for secondary prophylaxis for CAD and stroke. This trend is seen more in low and low middle-income countries. The data is robust and clearly shows correlation of usage of medications with economic status of a country. The data strongly argues for a concerted community level approach to address this issue which is the most cost effective strategy to improve cardiovascular outcomes in patients with established cardiovascular disease.

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