range of 35–45 years (even if he has both criteria) is only 34 in 100,000 or 0.03%.

Perspective

Previous studies by Tikkanen et al. (NEJM 2009;361:2529–37) reported that location of the early repolarisation pattern in the inferior leads and amplitude of the J-point elevation ≥ 0.2 mV had adverse prognostic value. This study adds ST-segment morphology analysis to risk stratify people with J-point elevation on ECG to differentiate 'benign' from 'malignant' form of early repolarisation syndrome.

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1. Randomised trial of ramipril in repaired tetralogy of Fallot and pulmonary regurgitation. The APPROPRIATE study (ACE inhibitors for potential prevention of the deleterious effects of pulmonary regurgitation in adults with repaired tetralogy of Fallot).

Babu-Narayan SV, Uebing A, Davlourous PA, et al.
Inter J Cardiol 2012;154:299–305.

doi: 10.1016/S0019-4832(12)60074-1

There is no consensus on optimal medical treatment and timing of pulmonary valve replacement for stable repaired tetralogy of Fallot (rTOF) patients with pulmonary regurgitation (PR) and consequent right ventricular (RV) dilatation. This randomised double-blind placebo study from United Kingdom aimed at studying the tolerability of the angiotensin-converting-enzyme (ACE) inhibitor, ramipril and its effect on cardiovascular function in rTOF patients. Clinically, stable rTOF patients with moderate/severe PR were included with 6 months follow-up. Cardiovascular magnetic resonance (CMR), echocardiography, neurohormonal analysis, and objective cardiopulmonary exercise testing were done at baseline and at follow-up.

Cardiovascular magnetic resonance-derived RV ejection fraction (EF) was considered the primary end-point. Seventy-two patients were enrolled of whom final analysis was performed on 64. Though, there was no difference in the primary end-point RV, i.e., EF, RV long-axis shortening improved significantly in the ramipril group compared to placebo (RV: 2.3 ± 3.8 vs 0.02 ± 2.7 mm; $P=0.017$) as did left ventricular (LV) long-axis shortening (1.9 ± 4.5 vs -0.2 ± 3.7 mm respectively; $P=0.030$). Other measurements did not differ in two groups. Patients on ramipril, compared to controls showed decrease in LV end-systolic volume index (-2.4 ± 5.0 vs 2.7 ± 3.6 mL/m²; $P=0.005$) and increase in LVEF (2.5 ± 5.0 vs -1.3 ± 3.5 ; $P=0.03$) in subgroup with restrictive RV physiology. Ramipril did not cause adverse events and was well-tolerated. Authors concluded that ramipril is a well-tolerated therapy, improves

biventricular function in patients with rTOF and may have a particular role in patients with restrictive RV physiology. Larger, longer term studies are needed to determine if ACE inhibitors can improve both ventricular remodelling and clinical outcomes.

Comment

Advances in diagnosis and management of congenital heart disease have resulted in an ever increasing adult cohort of rTOF patients. The PR subsequent to TOF repair though can be well-tolerated for several years, is a major cause of late morbidity in this population. Taking cues from beneficial effects of ACE inhibition in various conditions, authors undertook this randomised placebo-controlled study to look at tolerability, feasibility and efficacy of such therapy in these patients. Six months of ramipril therapy did not show improvement in RVEF. However, it was well-tolerated and did result in an increase in biventricular longitudinal systolic function. The ACE inhibition in patients with restrictive RV filling showed reduction in LVESVi and improvement in LVEF. Despite limited number of patients included, a relatively short follow-up and not so robust data to support benefit, this randomised trial has paved the path for future studies. This strategy of ACE inhibition, if found useful; can help deferring deleterious effects of PR in rTOF patients and thereby postponing pulmonary valve replacement.

2. Impact of the permanent ventricular pacing site on left ventricular function in children: a retrospective multicenter survey.

van Geldorp IE, Delhaas T, Gebauer RA, et al.
Heart 2011;97:2051–5.

doi: 10.1016/S0019-4832(12)60075-3

Chronic right ventricular (RV) pacing is associated with deleterious effects on cardiac function. This observational multicentre study by Geldrop et al. looked at the importance of the ventricular pacing site on left ventricular (LV) function in children with isolated atrioventricular (AV) block receiving chronic ventricular pacing. Demographics, maternal autoantibody status, and echocardiographic measurements on LV end-diastolic and end-systolic dimensions and volumes at age <18 years were collected retrospectively from patients who have undergone ventricular pacing >1 year ago for isolated AV block. The LV contractility was assessed using LV Fractional Shortening (LVFS) and, if possible LV ejection fraction (LVEF) analysis. Linear regression analyses were adjusted for patient characteristics. Two-hundred and ninety-seven children from 27 centres were included, in whom pacing was applied at the RV epicardium (RVepi, $n=147$), RV endocardium (RVendo, $n=113$) or LV epicardium (LVepi, $n=37$). LVFS was significantly affected by pacing site ($P=0.001$), and not by maternal autoantibody status ($P=0.266$). The LVFS in LVepi ($39 \pm 5\%$) was significantly higher than in RVendo ($33 \pm 7\%$, $P<0.001$) and RVepi ($35 \pm 8\%$, $P=0.001$; no significant difference between

RV-paced groups, $P=0.275$). Subnormal LVFS ($LVFS < 28\%$) was seen in 16/113 (14%) RVendo-paced and 21/147 (14%) RVepi-paced children, while LVFS was normal ($LVFS \geq 28\%$) in all LVepi-paced children ($P=0.049$). These results are supported by the findings for LVEF ($n=122$): LVEF was $< 50\%$ in 17/69 (25%) RVendo- and in 10/35 (29%) RVepi-paced patients, while LVEF was $\geq 50\%$ in 17/18 (94%) LVepi-paced patients.

Authors conclude that in children with isolated AV block, permanent ventricular pacing site is an important determinant of LV function, with LVFS being significantly higher with LV epicardial pacing than with RV pacing.

Comment

The pacing-induced activation pattern is characterised by prolonged total activation duration and an abnormal sequence of activation (in both longitudinal and transverse directions) which may lead to dyssynchronous ventricular contraction. The degree of dyssynchrony varies with the site of pacing.

The preservation of cardiac function during chronic ventricular pacing should be a high priority, especially in paediatric patients who are usually paced from an early age and may expect lifelong pacing. This study indicates that pacing site significantly influences LVFS, with better LVFS in patients with LV epicardial pacing compared to those with RV epicardial or endocardial pacing. The median follow-up of pacing in this study, as in other studies, was less than a decade, which is just a fraction of the life expectancy of a child receiving ventricular pacing for complete AV block. The index study, though retrospective, strengthens support to the use of LV pacing which incidentally is technically easier with lateral thoracotomy or subxiphoid approach.

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