Clinical characteristics and natural history of PRKAG2 syndrome

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On behalf of Clinical charactersitics and natural History of cardiac glycogenosis due to PRKAG2 mutations

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Purpose: Mutations in the PRKAG2 gene cause a syndrome characterized by hypertrophic cardiomyopathy, conduction disease and ventricular preexcitation. Only a small number of cases have been reported, and the natural history of the disease is poorly understood. The aim of this study is to describe phenotype and natural history of PRKAG2 mutation in a large multicenter international cohort.

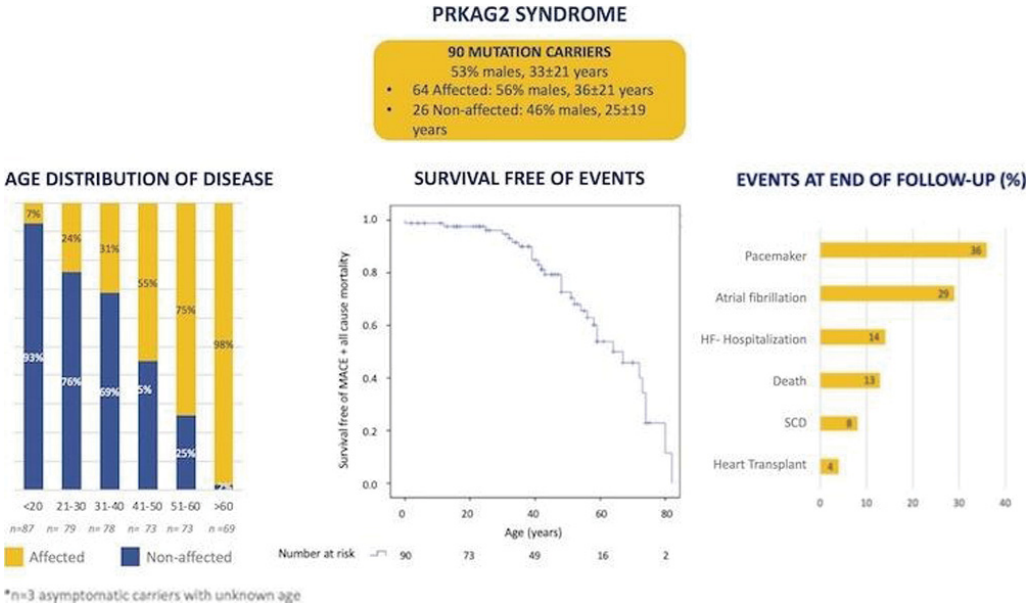
Methods: We retrospectively studied clinical, electrocardiographic and echocardiographic data from 90 individuals with PRKAG2 mutations (53% males, 33±21 years) from 27 centers.

Results: At baseline evaluation, 93% of patients were in NYHA functional class I-II. Maximum left ventricular (LV) wall thickness was 18±8 mm and LV hypertrophy (LVH) was present in 60 (67%) subjects at baseline. LV ejection fraction was 61±12%. Seventeen pactients (19%) had a pacemaker (mean age at implantation 37±15and 16 (18%) had atrial fibrillation (AF) (mean age 41±23 years) and 33% had ventricular preexcitation or had undergone an accessory pathway ablation. After a median follow-up of 6 years (IQR:2.3–13.9), 71% of individuals had LVH, 29% had AF, 21% a de novo pacemaker (mean age at implantation 38±18 years), 14% required admission for heart failure (HF), 8% experienced sudden cardiac death or equivalent, 4% required a heart transplant and 13% died.

Conclusions: PRKAG2 syndrome is a severe, progressive cardiomyopathy characterized by high rates of AF, conduction disease, advanced HF and life-threatening arrhythmias. Outcome is not clearly related to the classical features of preexcitation and severe LVH, which are not always present.

Clinical features at baseline evaluation

	Affected Carriers (n=64)	Non-affected Carriers (n=26)
Male Gender, n (%)	36 (56)	12 (46)
Age, years-old	36±21	25±19
Family History of sudden cardiac death, n (%)	24 (38)	11 (46)
Stroke, n (%)	4 (6)	0
Myopathy, n (%)	2 (3)	0
CK, U/L (range)	106 (2–365)	66 (2–130)
NT-proBNP, pg/ml (median, IQR)	170 (37–2168)	47 (10–224)
Pre-excitation, n (%)	30 (44)	0
QRS, ms	131±37	108±26
Atrial Fibrillation, n (%)	16 (25)	0
LV maximal wall thickness, mm	20±8	10±2
Left ventricular ejection fraction, %	60±13	66±8



Natural history of PRKAG2 syndrome