High prevalence of arrhythmic and myocardial complications in patients with cardiac glycosenosis due to PRKAG2 mutations: comment

We have read with great interest the article by Thevenon et al. The authors demonstrate a high risk of arrhythmic and myocardial complications in patients with PRKAG2 cardiomyopathy, which characterized by increased glycogen content. Having known the important role of PRKAG2 on the expression of the AMP-activated protein kinase (AMPK), this finding supports our opinion that AMPK-dependent glycolysis metabolism alterations are associated with the development of arrhythmia. Encoded by the PRKAG2 gene, the γ2-subunit is the energy sensor of the AMPK complex, a heterotrimERIC protein composed of α, β, and γ subunits. In our previous work, AMPK may play as a critical regulator in energy metabolic alterations during atrial arrhythmia. The main effects of AMPK depend on the isoforms of the catalytic AMPKα subunit. AMPKα2 is implied as a regulator of mitochondrial function through promoting glucose uptake, but AMPKα1 mainly promotes myofibroblast activity after chronic cardiac ischaemia. One research has found that AMPKα2 rather than AMPKα1 are the primary mediators of the effects of PRKAG2 mutations. In other words, the abnormal expression of γ2-subunit may influence the activity of AMPKα2, prior to AMPKα1. Thus, the myocardium histomorphological feature of PRKAG2 cardiomyopathy is the increased glycogen content within mitochondria, rather than abundant myofibroblast fibrosis.

Exercise has been proved to be benefit for better cardiac function in patients with cardiomyopathy. However, unlike other types of cardiomyopathy, exercise should be cautious for patients with PRKAG2 cardiomyopathy. Musi et al. discovered that AMPKα2 activity in the heart increased in response to acute exercise and that this isoform was more sensitive to the effects of exercise compared with AMPKα1. Having known the feature of AMPKα subunits in PRKAG2 cardiomyopathy, we give our opinion that exercise may further increase the activity of AMPKα2, and aggravate the glycogen deposition in mitochondria. The benefit for attenuate the myocardial fibrosis by activated AMPK is limited by the inaction of AMPKα1. Ahmad et al. have already found that PRKAG2 mutation has little effect on resting cardiac energy metabolism but accelerates the glycogen metabolism under exercise.

In conclusion, the histomorphological feature of PRKAG2 cardiomyopathy is dependent on the different affinity of the γ2-subunit to AMPKα1 and α2. Patients with PRKAG2 cardiomyopathy should avoid acute exercise.

Conflict of interest: none declared.

References


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doi:10.1093/europace/eux257 Published online 23 September 2017

High prevalence of arrhythmic and myocardial complications in patients with cardiac glycosenosis due to PRKAG2 mutations: Authors’ reply

We appreciate interest by Dr Liu and colleagues in our article and thank them for comments regarding our recently published article in Europace.

The purpose of our article was to describe our cohort of PRKAG2 cardiomyopathy patients and the clinical follow-up. We also wanted to stress the importance of a regular clinical care due to a high risk of arrhythmic complications.

The authors indicate that mutations in PRKAG2 are responsible for glycogen deposits within mitochondria and heart tissues. In a recent article, Hinson et al. showed that a specific mutation in PRKAG2 is responsible for an increase of mitochondrial biogenesis and a protection in development of cardiac fibrosis. In our article, no complete histomorphological analysis could be done in patients, as cardiac biopsy is not a routine exploration in France, but the presence of fibrosis at the cardiac level was observed by magnetic resonance imaging examination. This fibrosis is a non-specific feature observed in almost all patients with cardiomyopathies. The only biopsy that has been observed is a muscle biopsy which presented deposits of glycogen in accordance with other observations.

The authors should be prudent about considering that exercise has proved to be benefit in patients with cardiomyopathies. Several sports are restricted with this condition whatever the type of cardiomyopathy [hypertrophic cardiomyopathy (HCM), dilated cardiomyopathy (DCM), arrhythmogenic right ventricle cardiomyopathy (ARVC)]. Most of sudden deaths occurred during exercise especially in young people and the ESC guidelines on hypertrophic cardiomyopathy recommend avoiding competitive sports activities in patients.

Conflict of interest: none declared.

References


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doi:10.1093/europace/euy048 Published online 18 April 2018

Auxiliary vein access with or without venography: is this the dilemma in the ultrasounds era?

We read with great interest the article by Squara et al. “Self-taught auxiliary vein access without