To the Editor,

We recently read the article entitled “A case of hypertrophic and dilated cardiomyopathic sudden cardiac death: de novo mutation in TTN and SGCD genes” by Baydar et al. (1) published in the Anatolia Journal of Cardiology in late 2016 with great interest. We commend the authors for their contribution to improving our understanding of sudden cardiac death mechanisms and suggesting potential reasons for occurrence of the condition of genetic origin. We do, however, have a number of thoughts about the study, which are outlined below.

The authors mentioned de novo mutation in the sarcoglycan (SGCD) and titin (TTN) genes. The article fails to mention, however, the parent-based variant approach to analysis. In human genetic diseases, the term “de novo mutation” by definition refers to an alteration in a gene that is present for the first time in one family member as a result of a mutation in a germ cell of one of the parents or in the zygote itself. It is only by analyzing the parents that their true contribution to the disease burden can be proven (2).

Furthermore, in the discussion section, the authors mentioned population frequencies of 2 variants using Exome Aggregation Consortium (ExAC) browser data. If those variants are de novo, they should not be in genetic data browsers like ExAC (3). Moreover, variant TTN:c.21758T>C was previously identified by Pugh et al. (4). The team reported this variant with a different transcript (c.41249T>C, p.Ile13750Thr NM_133378.4), and it has been identified in 5 individuals with dilated cardiomyopathy (DCM) ranging in age from early infancy to mid 30s, with one individual in their 60s who has been diagnosed with hypertrophic cardiomyopathy (HCM) (4). Therefore, as these variants were identified by other research groups, they are no longer novel, as maintained in the current report.

Since only a single SGCD:c.15G>C variant with unknown significance was identified, it is not very likely that the SGCD gene is implicated in the pathology of this case. According to general variant classification assertion criteria, homozygous mutant allele of rs549319429 is classified as “likely benign” variant [December 8, 2015; GeneDx Variant Classification (06012015)] (5).

Sequencing of TTN gene revealed heterozygote TTN:c.21758T>C. Pugh et al. (4) described effect of this variant on both DCM and HCM in 2014 (4). Therefore, though SGCD:c.15G>C variant may be benign, in combination with possible pathogenic variant, such as TTN:c.21758T>C, clinical phenotype might produce an exponential effect.

To understand the certain effects of these variants on gene products, parent testing and co-segregation analyses should have been conducted before mentioning pathogenicity of the variants. Unfortunately, in the current article, it appears as though the authors have not completed any of these experiments.

Once again we would like to thank the authors and acknowledge their great efforts in presenting their case study. De novo mutation or pathogenicity of the variant family studies and segregation analysis should be conducted. Until these studies are completed the pathogenic effect of variants should not and cannot be mentioned.

Letter to the editor regarding the article “A case of hypertrophic and dilated cardiomyopathic sudden cardiac death: de novo mutation in TTN and SGCD genes” by Baydar et al. (1) published in the Anatolia Journal of Cardiology in late 2016 with great interest. We commend the authors for their contribution to improving our understanding of sudden cardiac death mechanisms and suggesting potential reasons for occurrence of the condition of genetic origin. We do, however, have a number of thoughts about the study, which are outlined below.

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References


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Author's Reply

To the Editor,

We are delighted with the interest shown in our work. In our article published in the Anatolia Journal of Cardiology in late 2016 entitled “A hypertrophic and dilated cardiomyopathic sudden cardiac death case; de novo mutations TTN and SGCD genes”, we demonstrated that the likely benign [NM_000337.5(SGCD):c.15G>C: (p.Glu5Asp)] and the missense [NM_003319.4(TTN):c.21758T>C (Ile7253Thr)] variants could be associated with dilated cardiomyopathy (DCM)/hypertrophic cardiomyopathy (HCM) as a cor bovinum disease or in young sudden cardiac death (1).

In the letter to the editor, it was claimed that our variant (TTN):c.21758T>C had been previously identified by Pugh et al. (2) and that therefore, the variant is no longer novel. However, this is immaterial because there is no such variant (TTN):c.21758T>C had been previously identified by Pugh et al. (2). We used the term “de novo” in our case report to mean a new instance, and perhaps were not attentive enough to its very specific genetic nomenclature. Regarding the comments on SGCD variant of “unknown significance,” there are many instances of single point mutations causing serious disease (e.g., sickle cell anemia). While we cannot definitively conclude that the mutation caused the heart pathology, we believe it is important to report this and similar cases, as these are relevant to whether these variants could merit further study. We agree that larger cardiologic clinical studies and sophisticated genetic studies carried out by specialists are required to clarify these issues. However, this lies outside the scope of the current work.

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Role of ABO blood groups in prosthetic valve thrombosis

To the Editor,

We read with great interest the article published in Anatolian Journal of Cardiology by Astarçıoğlu et al. (1) entitled “ABO blood types: impact on development of prosthetic mechanical valve thrombosis.” Several risk factors of prosthetic valve thrombosis (PVT) are well known. The search for new categories of risks should continue to refine even more the initial therapeutic decision in PVT. In this work, the authors evaluated the association between blood group status and PVT. They reported that patients with non-O blood groups have greater incidence of PVT compared with O blood groups. This result suggests that non-O group may be a risk factor that favors developing PVT.

It is increasingly recognized that individuals with non-O blood groups may be at elevated risk of venous and arterial thromboembolic events compared with individuals with blood group O. This increased risk has been attributed to higher concentrations of factor VIII and von Willebrand factor (2).