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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 (Ile-7253Thr)] 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 reported by Pugh et al. (2) (see Supplementary-1 Cases).

Although the genes NM_000337.5(*SGCD*):c.15G>C (p.Glu5Asp) and NM_003319.4(*TTN*):c.21758T>C (Ile7253Thr) were identified as likely benign and missense variants, respectively, in National Center for Biotechnology Information (NCBI) database and had not been previously reported as disease or death-causing variants, we found that titin (*TTN*) and sarcoglycan (*SGCD*) genes are associated with HCM/DCM and DCM, since cause of death was determined to be sudden circulatory failure resulting from DCM/HCM.

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 Astarcioglu 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).

Recently, Vasan et al. (3) published a study of 1.5 million blood donors in which they investigated the association between ABO blood groups and incidence of first and recurrent venous thromboembolic and arterial events. They concluded that the study added strong evidence of a consistent association between non-O blood groups and both venous thromboembolism and cardiovascular events. Taking into account that non-O blood groups confer an overall increased risk of incident, recurrent, and provoked thromboembolism, ABO blood group may have a role in thrombosis risk assessment and could potentially be added to available clinical prediction systems (3).

In the last 4 decades, several studies have investigated the importance of ABO blood group as risk factor of occurrence of arterial thrombosis. In general, a significant increase in the incidence of ischemic heart diseases and cardiovascular mortality in patients with non-O blood groups has been observed (4). One mechanism proposed to explain the association between ABO blood type and ischemic heart disease is elevated serum fibrinogen level. Elevated fibrinogen level constitutes a valuable marker in diagnosis of PVT (5).

It is a fact that patients with non-O blood group have a higher risk of developing venous and arterial thromboembolic events than members of the O blood group.

This report is the first that shows the association between the ABO blood types and occurrence of PVT.

Despite its limitations and need to occur more evidence on this topic, think that non-O blood groups can convert is in an attractive biomarker prognosis for in development of PVT.

In agreement with the authors, I suggest using ABO blood types as a new factor in the stratification of risk of thrombosis in patients with prosthetic heart valve.

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Author's Reply

Authors of this mentioned article did not send any reply for this Letter to Editor, in spite of our insistently request.

Heart rate variability in Eisenmenger syndrome and its correlation with echocardiographic parameters and plasma BNP, high sensitivity troponin-I level

To the Editor,

Eisenmenger syndrome (ES) is the latest stage of congenital heart disease associated pulmonary arterial hypertension (PAH) and is more common in our daily practice lately. Despite all improvements, there are several limitations to determining prognosis of these patients (1). Therefore, different parameters with high prognostic values are needed. Heart rate variability (HRV) and autonomic dysfunction can be early prognostic markers in patients with ES.

Twenty patients with ES (12 female, 8 male) and 20 healthy matched volunteers were enrolled in the study. Plasma brain natriuretic peptide (BNP) and troponin-I levels were measured. HRV parameters were calculated from 24-hour Holter electrocardiogram recordings. HRV parameters were compared with those of 20 healthy subjects. Bivariate analysis was performed to evaluate correlation between echocardiographic parameters and plasma BNP, high sensitivity (hs)-troponin-I levels. Mean age was 29.25±12.53 years and patients were clinically stable. All patients were receiving specific pulmonary hypertension treatment. Eight patients (40%) were receiving combination therapy, while 12 patients (60%) were receiving single agent.

There were significantly lower time-domain HRV parameters [SD of all RR intervals (SDNN): 125.8±36.96 vs. 173.30±34.47 (p<0.0001); mean of SD of all RR intervals for all 5-minute segments over the entire recording (SDNNi): 48.30±14.65 vs. 71.65±19.74 (p<0.0001); SD of averaged normal RR intervals calculated for all 5-minute periods (SDANN): 116.15±37.22 vs. 157.00±31.18 (p<0.0001); 32.25±14.32 vs. 39.05±14.98 (p=0.151); triangular index (TI): 40.31±20.05 vs. 48.45±14.16 (p=0.150)] in ES patients compared to healthy controls. Root-mean-square of successive normal sinus RR interval difference (RMSSD) and TI were lower in ES patients, but without statistical significance (p=0.151).