# The bicuspid aortic valve and arrhythmogenic right ventricular cardiomyopathy. Unreported coexistence

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## INTRODUCTION

The bicuspid aortic valve (BAV) is featured by the abnormal fusion of two leaflets of the aortic valve during development, leading later on in life to its degeneration and possible ascending aorta (AA) dilatation. Several classifications and terms have been proposed to describe BAV types (Schaefer, Sievers, and Kang classifications). The recently published International Consensus Statement on Nomenclature and Classification of BAV distinguishes three types of BAV with specific phenotypes [1].

Arrhythmogenic right ventricular cardiomyopathy (ARVC) is characterized by structural myocardial abnormality and is associated with malignant arrhythmias. ARVC predominantly affects the right ventricle (RV), but a broader spectrum of arrhythmogenic cardiomyopathy may involve both ventricles [2]. The 2010 revised Task Force Criteria for diagnosis of ARVC include electrocardiographic abnormalities, arrhythmias, structural abnormalities, tissue characteristics, genetics as well as family history (divided into major and minor criteria) — see Marcus et al. [3] (Table 1 from [3]). As discussed in a very insightful review of ARVC, sensitive diagnostic criteria still need to be improved [4].

BAV and ARVC usually have autosomal dominant inheritance patterns described in detail elsewhere. Briefly, BAV is characterized by a low penetrance and variable expression [5] and is attributed to a wide spectrum of gene mutations (related to syndromic and non-syndromic forms) [6]. ARVC is associated mostly with pathogenic variants in desmosomal genes, accounting for over 50% of cases in its classical form, with plakophilin-2 gene (*PKP2*) mutations being the most frequent [7]. Thus, the common pathogenesis of these disorders is unlikely.

BAV is the most common congenital heart anomaly (a prevalence of around 1%–2% in the general population), while ARVC is a much less frequently encountered disease (a prevalence of 0.02%–0.1%) [8].

To our best knowledge, the coexistence of these two diseases has not been reported so far. We present two male patients with both of these anomalies.

## METHODS

We retrospectively screened the echocardiographic reports of 155 ARVC patients filed in an electronic database from a tertiary high-volume heart center. This database contains reports on echocardiographic examinations from January 2008 to the present. Nonetheless, some of these patients were diagnosed with ARVC before 2008 and thus were followed up for a longer time.

## RESULTS AND DISCUSSION

Two male patients with ARVC and coexisting BAV were identified.

In both patients, ECG (depolarization and repolarization abnormalities, Supplementary material, *Figures S1* and *S2*) and genetic examinations (mutations in *PKP2*) fulfilled the criteria for diagnosis of ARVC. Types of pathogenic variants were as follows: patient 1 — p.His318TrpfsTer10 c.929_951dupTGGATTCCAGCGGGAGGAGAGCG(rs1064792927); patient 2 — c.2489+1G>A (rs111517471).

### Patient 1

The patient was diagnosed with ARVC at the age of 33 years. His familial history included sudden cardiac death of his father at the age of 33 years and ARVC in his sister. At that time, transthoracic echocardiography (TTE) showed preserved systolic function of the left ventricle (LV). Six years later he underwent implantation of an implantable cardioverter-defibrillator in the primary prevention of sudden cardiac death. The same year and six years later radio-frequency ablations were performed for ventricular arrhythmia. His recent TTE showed significantly impaired systolic function of both ventricles (left ventricular ejection fraction [LVEF], 30%; RV S', 6 cm/s), dilated RV (inflow tract 59 mm) with free wall trabeculae, very large secondary tricuspid regurgitation, and paradoxical interventricular septal motion. Additionally, a fusion of the non-coronary aortic leaflet with right coronary aortic leaflet together with small aortic regurgitation and slight AA dilatation (38 mm) were visualized (Supplementary material, *Figure S3A*). Computed angiography showed discrete irregularities of the coronary arteries and confirmed the presence of BAV (Supplementary material, *Figure S3C* and *S3D*). In the following year, several exacerbations of heart failure and electrical storms were observed. Finally, at the age of 56 years, he underwent successful orthotopic heart transplantation. During the 3-year follow-up, he remained in stable condition.

### Patient 2

A 59-year-old patient with ARVC, ventricular arrhythmias, resistant arterial hypertension, and obesity was admitted to the hospital with the first episode of atrial fibrillation (AF). Recent TTE showed dilated RV (inflow tract 53 mm, outflow tract 42 mm) with impaired systolic function (RV S' 7–9 cm/s), non-significant tricuspid regurgitation with the enlarged right atrium (area 28 $cm^2$). The hypertrophied (13 mm) LV had preserved systolic function. Fusion of non-coronary aortic leaflets with right coronary aortic leaflets, small aortic regurgitation, and moderate AA dilatation (49 mm) were visualized. After pharmacological treatment atrial fibrillation resolved within one day. Oral anticoagulant treatment (rivaroxaban) was initiated.

ECG abnormalities are shown in Supplementary material, *Figure S3*.

The different phenotype of both entities is indisputable. Nonetheless, several points are worth emphasizing.

### Type of BAV

Both patients had a fusion of the non-coronary leaflet and right-coronary leaflet, which is not typical of BAV in the general population. False (with raphe) BAV with a fusion of the coronary cusps (left to right) represents up to 80% of cases of BAV [9].

### Aortopathy

No association of ARVC with aortic dilatation (typical of BAV) has been described so far. However, ARVC patients with chronic aortic dissection and degenerative changes in the media of the aorta (as seen on autopsy) were reported [10].

### Ventricular function in both diseases

Biventricular involvement in ARVC is frequent. A small MRI study showed that LV involvement among patients with arrhythmogenic cardiomyopathy was common [11]. Still, only mild LV systolic dysfunction was observed in most of these patients (as opposed to our first patient). ARVC may also be associated with only regional LV dysfunction [12]. BAV is not typically associated with significant LV systolic dysfunction although mild LVEF reduction was observed in previous studies [13]. Other myocardial anomalies may be associated with BAV. In a large Korean registry of 1186 patients with BAV, 5.6% of them had concomitant cardiomyopathies (most frequently LV non-compaction — 3.4%, followed by hypertrophic cardiomyopathy — 1.4%, and dilated cardiomyopathy) [14].

### Prevalence

The prevalence of BAV in a relatively large cohort of our ARVC patients was 1.29% (2/155). This is similar to the prevalence of BAV in the general population. Thus, a more than casuistic coexistence of BAV and ARVC cannot be demonstrated or excluded in these cases.

### Clinical relevance of BAV in patients with ARVC

Our second patient presented with moderate AA dilatation (below the threshold for preventive aortic surgery). As is known from their histories, most probably more than 50% of patients with BAV will undergo intervention for BAV (due to BAV stenosis or regurgitation) during their lifetime. Moreover, dilatation of the AA will require aortic surgery in more than 25% of these patients [15]. Cardiothoracic surgery in patients with ARVC may be associated with increased perioperative risk.

### Limitations

The retrospective nature of the study carries inherent limitations. We did not specifically analyze every TTE (or transesophageal echocardiography in some cases), but instead, we searched specific keywords (BAV with its grammatical variations).

## CONCLUSIONS

The coexistence of BAV and ARVC most probably has not been reported before. The accidental coexistence of these two anomalies can neither be confirmed nor excluded.

### Supplementary material

Supplementary material is available at https://journals.viamedica.pl/kardiologia_polska

## *Article information*

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