Tetralogy of Fallot and bicuspid aortic valve: Rare coexistence

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INTRODUCTION

Bicuspid aortic valve (BAV) is one of the most frequent cardiovascular anomalies (prevalence 0.5%–2.0%) [1]. Briefly, multiple classifications and nomenclature have been previously proposed to describe the BAV types (Sievers, Schaefer, and Kang classifications). The recently published International Consensus Statement on Nomenclature and Classification of BAV distinguishes three types of BAV with specific phenotypes [2].

Tetralogy of Tallot (ToF) constitutes around 10% of all congenital heart diseases (CHD). The prevalence in general population is around 0.03% [3]. Recently Grzyb et al. [4] presented a very insightful analysis of the largest single-center cohort of 326 ToF fetuses.

Numerous papers have reported the association of BAV with other CHD, as well as extra-cardiac anomalies. However, only a few reports on the coexistence of BAV and ToF have been published so far. Most of them included pediatric patients and not adults (Supplementary material, *Table S1*), and usually did not have any details regarding the BAV type. Based on the very scarce data, the prevalence of BAV ranges between 0.2% and 2.4% in pediatric ToF cohorts and 2.0% in two cohorts of adult ToF patients (Supplementary material, *Table S1*).

Aim

We aimed to retrospectively identify BAV among the cohort of ToF patients.

METHODS

We retrospectively screened discharge summaries from an electronic database of a tertiary high-volume heart center. In the studied period (January 2008 to November 2020), 103 330 patients were hospitalized; among them — 564 ToF patients. The keywords: "tetralogy of Fallot" and "bicuspid aortic valve" (with their grammatical variants and abbreviations) were used to identify ToF and BAV.

Statistical analysis

Statistical analysis was limited to the simple calculation of the prevalence of BAV among all hospitalized ToF patients.

RESULTS AND DISCUSSION

Three patients (including one female) with ToF and BAV were identified. All of them underwent several transthoracic echocardiographic (TTE) examinations.

Patient 1 (MZ)

The first patient was a 40-year-old female after surgical correction of ToF (right ventricular outflow tract correction with a pericardial patch) at the age of three years, with ventricular arrhythmias treated with propafenone. She remained in functional class II according to the New York Heart Association. Her recent TTE revealed hypokinetic right ventricle (RV): tricuspid annular plane systolic excursion, 16 mm; RV, S' 7 cm/s, moderate pulmonary regurgitation (PR), dilated aortic root (44 mm),

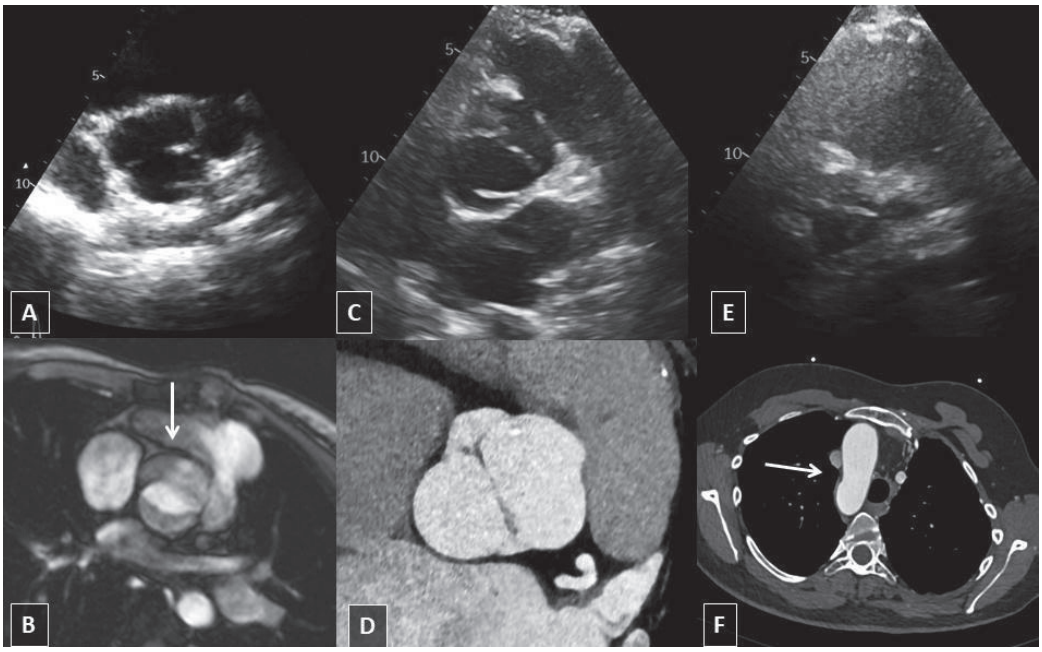

Figure 1. A, C, E. Patients 1–3, respectively. Echocardiography. The bicuspid aortic valve with fused coronary cusps. **B.** Patient 1. Cardiac magnetic resonance with focus on the bicuspid aortic valve (the white arrow). **D.** Patient 2. Chest computed tomography. The bicuspid aortic valve without raphe. **F.** Patient 2. Chest computed tomography. The right aortic arch (the white arrow)

and mild dilatation of the ascending aorta (AAo), 40 mm. Systolic function of the non-dilated left ventricle (LV) was preserved. The fused BAV type (right-left cusp fusion) was diagnosed (Figure 1A). Cardiac magnetic resonance (CMR) performed at the age of 32 years showed moderate to severe PR and a moderately enlarged RV with good contractility and confirmed the presence of BAV (Figure 1B). Peak oxygen uptake was 26 ml/min/kg (74% of value according to age and sex) on the cardiopulmonary exercise test. Conservative treatment was continued.

Patient 2 (ML)

The second patient was a 36-year-old male after total correction of ToF at the age of five years, with extreme hypoplasia of the left pulmonary artery, hypoplasia of the left lung (vascularized from the left internal thoracic artery, and bronchial and intercostal arteries), AAo dilatation, right-sided aortic arch (RAA) with a ductus diverticulum, persistent left superior vena cava, and paroxysmal supraventricular tachycardias. Recent TTE showed a dilated RV (RV inflow tract, 58 mm; RV outflow tract, 47 mm; RV area, 45 cm^2), significant PR, moderate tricuspid regurgitation (tricuspid regurgitation pulmonary gradient 49 mm Hg), enlarged right atrium (RA); area 29 cm^2, dilated both the aortic root (47 mm) and AAo (39 mm). Systolic function of both ventricles was preserved. The fused BAV type (right-left cusp fusion) was diagnosed and confirmed by chest computed tomography (CT) (Figure 1C). One year earlier, he had been offered a radio-frequency ablation of the arrhythmia substrate, to which he did not consent. No indication for the surgical correction of PR was established, and the limitation of exercise tolerance and paroxysmal dyspnoea were believed to be related to left lung hypoplasia.

Patient 3 (SW)

The third patient was a 48-year-old male after central pulmonary anastomosis at the age of 11 years and complete correction of ToF at the age of 32 years, with a significant shunt through re-ventricular septal defect with Qp/Qs 2:1 on the right heart catheterization, permanent atrial fibrillation, bifascicular block, and arterial hypertension. He was offered redo surgery. Preoperative TTE showed interventricular residual shunt in the lower part of the patch with a left-to-right gradient of 78 mm Hg, dilated and hypokinetic RV (RV inflow tract 59 mm, RV outflow tract 43 mm, RV S' 9 cm/s), mild tricuspid regurgitation (RV systolic pressure 93 mm Hg), enlarged RA (area 40 cm^2), dilated pulmonary trunk (27 mm), enlarged left atrium (area 38 cm^2), dilated both the aortic root (49 mm) and AAo (45 mm). The left ventricle was non-dilated with preserved systolic function. The fused BAV type (right-left cusp fusion) was diagnosed (Figure 1E). He underwent mechanical aortic valve implantation — St. Jude Medical Regent 27 mm (St. Jude Medical, Inc, St. Paul, MN, US) with closure of the re-ventricular septal defect using an artificial patch and surgery of the aortic root. The presence of BAV was confirmed intraoperatively. Postoperative TTE showed a reduction in the right ventricular systolic pressure (43 mm Hg).

Only small regurgitation of the aortic valve was visible in all these patients. In none of them, was trans-valvular gradient measured nor coarctation of the aorta diagnosed.

Firstly, all our patients presented with mild to moderate dilatation of the aortic root (40 mm, 47 mm, and 49 mm, respectively) and ascending aorta (40 mm, 39 mm, and 45 mm, respectively), without significant progression over time (Supplementary material, *Table S2*). Arterial hypertension (third patient) could contribute to AAo dilatation. Dilatation of the proximal AAo is frequent in BAV patients (20%–68%) [5]. Notably, most adolescents with repaired ToF and tricuspid aortic valve (TAV) show also significant dilatation of the aortic root and AAo [6, 7]. Assessment of AAo in ToF patients with BAV is limited to one study [7]. It revealed that aortic dissection did not occur in ToF patients with significant aortic aneurysms. Thus, AAo-diameter thresholds might be higher for ToF patients while considering prophylactic AAo surgery (taking into account the increased risk of re-operation). Already, all of our three patients underwent corrective surgery for ToF in the past. There was no availabe data about the risk of aortic dissection in ToF patients (usually after previous surgeries) with AAo-dilatation and BAV. Thus, the decision regarding prophylactic aortic surgery should be individualized.

Secondly, all our patients presented with the fused type of BAV, with right-to-left leaflet fusion. The quality of the echocardiographic examination in patients after previous cardiac surgeries may be suboptimal. Thus, accurate characterization of BAV morphology and the unambiguous assessment of the presence of raphe may be difficult. Other imaging modalities (CT, CMR) may give insight. A retrospective study of 156 adult patients has shown that right-to-left leaflet fusion was strongly associated with rapid aortic dilatation [5].

Thirdly, patient 2 presented with RAA (Figure 1F). The prevalence of RAA in the general population is very low (ranging between 0.04% and 0.1% [8, 9]); however, it is not a rare finding in ToF cohorts (around 20% [10]). Apart from ToF, the separate coexistence of BAV and RAA is a casuistic finding (Supplementary material, *Table S3*).

Finally, the prevalence of BAV among adult ToF patients (0.53%) is similar to the prevalence in the general population.

Limitations

Retrospective nature carries inherent limitations. We did not specifically analyze every imaging examination (echocardiography, chest CT, CMR) of ToF patients, but instead, we searched for specific keywords in our electronic database of discharge summaries. Secondly, two of three patients underwent surgical correction at an early age (in another hospital). Thus, we did not have a detailed report of the operation. Finally, the number of patients was small, and thus the statistical analysis was limited to the prevalence of BAV among ToF.

CONCLUSIONS

These three patients add to the very limited literature on BAV among ToF patients. The previous reports were focused on the casuistic coexistence of these two anomalies and mainly in the pediatric population. This paper presents the first systematic study of BAV among a large cohort of adult patients with ToF, providing additional new findings, namely the BAV type, as well as information on the prevalence of BAV among the ToF cohort.

Article information

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