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). 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 ranging from 0.03% to 2.8% [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 few reports of the coexistence of BAV and ToF were published so far. Most of them included pediatric patients and not adults (Supplementary material, Table S1), and usually without any details regarding 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**
To retrospectively identify BAV among the cohort of ToF-patients.

**METHODS**
We retrospectively screened the discharge summaries filled in the electronic database from 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 variations 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 (one female) with ToF and BAV were identified. All of them underwent several transthoracic echocardiographic (TTE) examinations.

**Patient 1 (MZ)**
A 40-year-old female patient after surgical correction of ToF (right ventricular outflow tract correction with pericardial patch) at the age of three years, with ventricular arrhythmias treated with propafenone. She remained in functional class II according to New York Heart Association. Her recent TTE revealed hypokinetic right ventricle (RV), (tricuspid annular plane systolic excursion tricuspid annular plane systolic excursion16 mm, RV S’ 7 cm/s), moderate
pulmonary regurgitation (PR), dilated aortic root (44 mm) 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 revealed 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)
A 36-year-old male patient after total correction of ToF at the age of five years, 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 dilated RV (RV inflow tract 58 mm, RV outflow tract 47 mm, RV area 45 cm²), significant PR, moderate tricuspid regurgitation (tricuspid regurgitation pulmonary gradient 49 mm Hg), enlarged right atrium (RA), (area 29 cm²), 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 was offered a radio-frequency ablation of the arrhythmia substrate, for which he did not consent. No indication for the surgical correction of PR was established, and the limitation of exercise tolerance and paroxysmal dyspnoea are believed to be related to left lung hypoplasia.

Patient 3 (SW)
A 48-year-old male patient after central pulmonary anastomosis at the age of 11 years and complete correction of ToF at the age of 32 years, 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 cm²), dilated pulmonary trunk (27 mm), enlarged left atrium (area 38 cm²), dilated both the aortic root (49 mm) and AAo (45 mm). Left ventricle was non-dilated with preserved systolic function. The fused BAV type (right-left cusp fusion) was diagnosed. 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. Presence of BAV was confirmed intraoperatively. Postoperative TTE showed 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 trans-valvular gradient was measured nor coarctation of the aorta was 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 much progress over time (Supplementary material, Table S2). Arterial hypertension (third patient) could contribute to the AAo-dilatation. Dilatation of the proximal AAo is frequent in BAV-patients (20%–68%) [5 and others]. 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 increased risk of re-operation). Already, all of our three patients underwent corrective surgery of ToF in the past. Nothing is known 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 the BAV morphology and the unambiguous assessment of the presence of raphe may be difficult. Other imaging modalities (CT, CMR) may give additional insight. 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. Prevalence of RAA in general population is very rare (ranging between 0.04%–0.1% [8, 9]), however is not a rare finding in ToF cohorts (around 20% [10]). Apart from ToF, 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 general population.
Limitations
Retrospective nature carries inherent limitations. We did not specifically analyzed every imaging examinations (echocardiography, chest CT, CMR) of ToF patients, but instead we searched for specific key-words in our electronically stored database of discharge summaries. Secondly, two of three patients underwent surgical correction at the early age (in another hospital). Thus, we do not have detailed report of the operation. Finally, the number of the patients is small, and thus the statistical analysis is limited to the prevalence of BAV among ToF.

CONCLUSIONS
These three patients add to the very limited literature of BAV among ToF patients. The previous reports were focused on the casuistic coexistence of these two anomalies and mainly in 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 the information on the prevalence of BAV among the ToF cohort.

REFERENCES


Figure 1. A–C. Patients 1–3, respectively. Echocardiography. Bicuspid aortic valve with fused coronary cusps. D. Patient 1. Cardiac magnetic resonance with focus on the bicuspid aortic valve (white arrow).