

### Atypical Cardiac Features in Patients with Noonan Syndrome

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**Background:** Noonan Syndrome (NS) is a relatively common autosomal dominant disorder with typical congenital heart defects (CHDs) such as pulmonary valve stenosis, hypertrophic cardiomyopathy and septal defects. Atypical cardiac features (ACF) are also rarely described in literature. Aim of this study was to report the prevalence and the outcome of these ACF in our population of patients affected by NS.

**Design and Methods:** A retrospective, multicentric, observational study was performed. All clinical and surgical data of NS patients followed until April 2017 at Bambino Gesù Children's Hospital and Department of Pediatrics - "Sapienza"- University of Rome, were collected. Molecular analysis was performed in all patients.

**Results:** A total of 208 patients with clinical diagnosis of NS were enrolled: 117 males and 91 females. In 167 patients a mutation of one of the known genes was reported: PTPN11, SOS1, RAF1, RIT1, SHOC2, BRAF, KRAS, NRAS, HRAS, CBL and LZTR1. CHDs were reported in 181 patients: 159 presented typical CHDs while ACF were described in 96 patients (isolated or combined with typical CHDs). Mitral, tricuspid and aortic valve were abnormal in 65, 22 and 35 patients, respectively; ascending and descending aorta were abnormal in 17 patients. Eight patients presented coronary dilatation while 1 patient had coronary stenosis; dilatation of left auricle was described in 3 patients. Tetralogy of Fallot (TOF) was described in 1 patient. Mutations of genes reported in patients with ACF were: PTPN11 (45,8%), SOS1 (12,1%), RAF1 (5,2%), BRAF (2,1%), RIT1 (5,2%), KRAS (1%), SHOC2 (4,2%), CBL (1%), NRAS (1%), HRAS (1%), LZTR1 (1%). Twenty patients with ACF had no known mutations (20,8%). Cardiac surgery was performed in 10 patients: 5 end-to-end anastomosis, 2 aortic replacement, 1 coronary stenosis dilation, 1 cardiac surgery for TOF and 1 mitral valve treatment. This last patient occurred a second intervention for mitral valve replacement. No patients died in our cohort.

**Conclusions:** Patients with NS usually present a typical spectrum of CHDs. Our data suggest that also ACF must be carefully identified for the possible impact on the clinical outcome of these patients.