**Methods:** From January 2004 to December 2009, 425 consecutive patients underwent a surgical AVR for isolated AS with a biological or mechanical prosthesis: BAV = 135 patients (31.8%), TAV = 290 patients (68.2%). Exclusion criteria included coronary artery disease and associated significant valvulopathy. Patients who underwent the Ross procedure (national referrals) or a transcatheter AVR (program started in 2010) were also excluded to avoid any selection bias.
**Results:** BAV patients were younger than TAV patients (61 years vs 75 years, $p<0.001$). Mean gradient was higher in BAV vs TAV (54 mmHg vs 50 mmHg respectively, p=0.049). At the time of surgery, the proportion of patients with decreased LVEF (<45%) was higher in the BAV group compared to the TAV group: 16.3% (22/135) vs 8.9% (26/290) respectively, p=0.026. LV dilatation was also more frequent in the BAV group (22.3% vs 14%, p=0.037). The overall early mortality rate after AVR was 3.7% (16/425), without significant difference between the 2 groups.
**Conclusion:** Our study shows that patients with stenotic BAV are at risk of impaired LV systolic function before surgical AVR compared to TAV patients, despite a younger age and a similar clinical tolerance. This adds to the fact that BAV is associated with an intrinsic cardiomyopathy. Further investigations are needed to determine more accurate criteria for the indication of AVR in this population.

## P672
## Bicuspid aortic valve in MFS patients: an incidental association

O. Milleron[1], F. Arnoult[2], M. Langeois[1], M. Tchitchinadze[1], J. Ropers[3], C. Bouleti[1], C. Boileau[4], G. Jondeau[1]. *[1]Hospital Bichat-Claude Bernard, Centre National de Réference pour le Syndrome de Marfan, Paris, France; [2]Hospital Bichat-Claude Bernard, Service des explorations fonctionnelles, Paris, France; [3]University Hospital Ambroise Pare, Unité de recherche clinique, Boulogne-Billancourt, France; [4]Hospital Bichat-Claude Bernard, Service de génétique, Paris, France*

**Background:** Prevalence of bicuspid aortic valve has been reported to be increased in Marfan (MFS) patients, and may carry additional aortic risk.
**Purpose:** We thought to evaluate the relation between FBN1 mutation and BAV in a large cohort of MFS patients.
**Method:** All patients with identified FBN1 mutation (FBN1+) evaluated in our clinic since 1996 were included. BAV was classified using 1) the Sievers classification and 2) as typical (anteroposterior valve opening with or without raphe) or atypical (lateral valve opening). Maximal aortic diameter and aortic valve morphology was measured with TTE at each visit.
**Results:**
– Prevalence: Out of the 1437 MFS patients with FBN1 mutation, 26 patients (1.8%) had a BAV. Predominance of male sex was observed with 18/26 males (69.2%) in the BAV group vs 680/1411 males (48.2%) of MFS with tricuspid aortic valve (TAV).
Prevalence of BAV type 1, i.e. one raphe (46% of BAV, all L-R) and type 0, i.e. no raphe (48% of BAV, 8 anteroposterior and 5 lateral) were similar. Typical BAV were significantly more frequent (20/26) than atypical BAV (5/26), p=0.01 (Figure). In one patient type of BAV remained undetermined.
– Association of BAV type and genotype: 13 patients (50%) were positive for a PTC mutation causing haploinsufficiency (reduced fibrillin-1 protein) and 13 (50%) for a missense mutation possibly leading to a dominant negative effect (abnormal fibrillin-1 protein). No difference in the type of BAV (either using Sievers classification or typical vs atypical) was observed between the 2 groups.
– Familial transmission: The FBN1 gene mutation was a de novo mutation in 8 patients and was inherited in 17/26 patients (in one patient, parental status for FBN1 gene mutation remained unknown). Ten were inherited from the mother and 7 from the father with no relation with the type of BAV.
BAV was present in another family member in only one family out of 14 families with more than one Marfan patient: Marfan brother and sister had a similar type 1 L-R BAV; however, the absence/presence and type of BAV in their affected father will remain unknown because Bentall surgery was performed 25 years earlier with no description of aortic valve morphology on the surgical report. No other BAV was observed in any of the 37 first degree relatives of other BAV patients screened in our clinic.

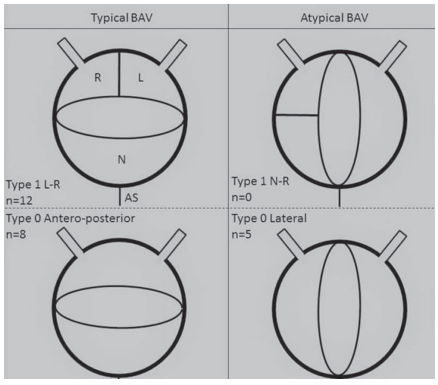


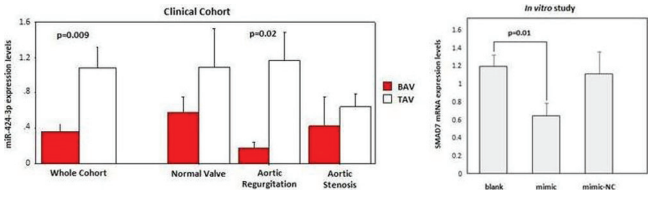
Figure 1

**Conclusion:** BAV is not more prevalent in MFS than in the general population and there is no FBN1 genotype / BAV phenotype correlation. Besides, BAV transmission is rare even in family members with FBN1 mutation. These results suggest that the association BAV and MFS is incidental.

## P673
## Circulating miR-424-3p is a promising biomarker of bicuspid aortic valve (BAV)-associated aortopathy by directly targeting SMAD7

S. Pulignani[1], A. Borghini[1], I. Foffa[2], C. Vecoli[1], L. Ait Ali[1], M.G. Andreassi[1]. *[1]Institute of Clinical Physiology, CNR, Pisa, Italy; [2]Institute of Clinical Physiology (IFC), Massa, Italy*

**Background:** Compelling evidence have shown that microRNAs (miRNAs) may be involved in the pathophysiology of BAV-associated aortopathy.
By analyzing the whole miRNome using small RNA sequencing, we have recently identified asignificant down-regulation of miR-424-3p in thoracic aortic aneurysm (TAA) specimens of BAV patients compared to TAV patients.
However, its clinical role and the functional mechanism needs to be further defined.
**Purpose:** To assess the circulating miR-424-3p as a potential biomarker of BAV-associated aortopathy as well as elucidate its biological functionin the pathogenesis of aneurysms.
**Methods:** A cohort of 24 patients with BAV (20 males; 53±13years) and 31 patients with TAV (24 males; 68±9 years) was enrolled. Plasma samples were taken preoperatively, and circulating miR-424-3p expression levels were measured by using qRT-PCR.
Functional analysis of miR-424-3p was assessed by transfecting synthetic miRNA mimic and inhibitor into human aortic vascular smooth muscle cells (HASMCs). The expression levels of miRNA-424-3p and SMAD7 mRNA were subsequently detected by qRT-PCR.
**Results:** Circulating levels of miR-424-3p were significantly down-regulated in BAV patients as compared to TAV (1.08±1.28 vs 0.36±0.37; p=0.009). Similarly, miR-424-3p was different expressed in plasma samples of BAV patients after stratification for aortic complications (see Figure).
miR-424-3p expression in HASMCs showed a significantly increase compared to blank control after transfection (3.67±0.29 vs 0.001±0.0003; $p<0.001$). Moreover, in vitro study revealed that SMAD7 mRNA expression was significantly decreased in miR-424-3p mimic transfected cells compared to blank control (1.19±0.13 vs 0.64±0.14; p=0.01) (see Figure).




**Conclusions:** Our results demonstrated that circulating miR-424-3p is a potential biomarker of BAV-associated aortopathy. Causal involvement of miR-424-3p in pathogenesis of aortopathy was found in HASMCs by targeting SMAD7 gene, an important mediator of TGF-β signaling pathway.

## P674
## Evaluation of sex differences in aortic valve dysfunction and aorta dilation in patients with bicuspid aortic valve

I. Dentamaro[1], L. Galian[1], F. Calvo[2], S. Moral[3], J. Robledo-Carmona[4], V. Sanchez[5], D. Saura[6], R. Arnold[7], R. Citro[8], A. Moreo[9], F. Chirillo[10], P. Colonna[11], G. Teixido[1], J. Rdriguez-Palomares[1], A. Evangelista[1]. *[1]University Hospital Vall d'Hebron, Department of Cardiology, Barcelona, Spain; [2]University Hospital Gregorio Maranon, Madrid, Spain; [3]University Hospital de Girona Dr. Josep Trueta, Girona, Spain; [4]University Hospital Virgen de la Victoria, Malaga, Spain; [5]University Hospital 12 de Octubre, Madrid, Spain; [6]Hospital Clínico Univeristario Virgen de la Arrixaca, Murcia, Spain; [7]Institute of Heart Sciences (ICICOR), Valladolid, Spain; [8]AOU S. Giovanni e Ruggi, Salerno, Italy; [9]Niguarda Ca' Granda Hospital, Milan, Italy; [10]Bassano del Grappa General Hospital, Bassano Del Grappa, Italy; [11]Polyclinic Hospital of Bari, Bari, Italy*

**Introduction:** Bicuspid aortic valve (BAV) is frequently associated with a significant valvular dysfunction and proximal aorta dilation. It is known that associations among valve morphotypes, cardiovascular risk factors and hemodynamic conditions may help to stratify the risk of aortic complications in these patients, but little is known regarding sex differences. The aim of this study was to assess sex differences in a large series of BAV patients.
**Methods:** A prospective cross-sectional echocardiographic study was conducted in 1020 consecutive adults (mean age: 48±16 years; 70% male) diagnosed of BAV, referred from cardiac outpatient clinics to echocardiographic laboratories. Exclusion criteria were aortic coarctation, other congenital disorders or valvular intervention. BAV morphotype, significant valve dysfunction and aorta dilation at sinuses and ascending aorta were established.
**Results:** 716 patients were male (70.2%). No differences were found between