

# Argentine Registry of Valvular Heart Diseases (ARGENVAL)

## Registro Argentino de Enfermedades Valvulares (ARGENVAL)

JUAN BENGER<sup>1</sup>, IVÁN CONSTANTIN<sup>1</sup>, MARÍA C. CARRERO<sup>1</sup>, SILVIA MAKHOUL<sup>1</sup>, SERGIO BARATTA<sup>1</sup>, FEDERICO CINTORA<sup>1</sup>, RODRIGO P. BAGNATI<sup>1</sup>. EN REPRESENTACIÓN DEL GRUPO DE ESTUDIO DEL REGISTRO ARGENVAL

### ABSTRACT

**Background:** Valvular heart disease is a prevalent pathology with considerable morbidity and mortality. Despite it represents a well-known public health problem, there is no epidemiological data available in our country. The aim of this study was to assess the prevalence and etiology of valvular heart disease in ambulatory patients referred for transthoracic echocardiography.

**Methods:** A retrospective, observational and multicenter registry was carried out with the participation of 18 Argentine centers. All patients underwent a complete transthoracic echocardiogram, in which the analysis of valvular function was performed by qualified operators. Demographic variables, causes and degree of valvular function involvement were collected.

**Results:** A total of 3020 patients (51.2% male) with mean age of 58.2±16.8 years were included in the study. In 61.7% of patients some degree of valvular abnormality was observed; in 9.5 % of cases at least one significant valve disease (moderate or greater) and in 1.7% a significant combined valve disease was observed. Four percent of the population had significant aortic stenosis, which was the most common major valve disease, followed by mitral regurgitation (2.9%) and tricuspid regurgitation (2.3%). The most frequent cause of aortic and mitral valve defect was degenerative and functional for significant tricuspid regurgitation. Significant heart valve disease increased notably with age, affecting 23.5% of patients older than 75 years. Mitral stenosis and tricuspid regurgitation were more frequent in female patients, with no gender differences in aortic valve disease and mitral regurgitation.

**Conclusions:** Valvular heart diseases were a frequent finding in our population and their prevalence increased with age. Degenerative etiologies were the main cause of aortic and mitral valve involvement, while a functional etiology was responsible for most cases of tricuspid regurgitation. Gender-specific patterns were observed for mitral stenosis and tricuspid regurgitation. Our findings provide relevant unique data on the epidemiology of heart valve disease in Argentina.

**Keywords:** Heart valve diseases - Epidemiology - Echocardiography - Argentina

### RESUMEN

**Introducción:** La enfermedad valvular constituye una patología prevalente y con considerable morbimortalidad. A pesar de que presenta una problemática de salud pública reconocida, en nuestro país, no disponemos de datos sobre su epidemiología. El objetivo del trabajo fue identificar la prevalencia y etiología de las enfermedades valvulares en los pacientes que concurren a los laboratorios de ecocardiografía en forma ambulatoria.

**Materiales y métodos:** Se realizó un registro retrospectivo, observacional y multicéntrico, en el que participaron 18 centros de Argentina. A todos los pacientes se les realizó un ecocardiograma transtorácico completo, en el cual el análisis de la función valvular fue realizado por operadores calificados. Se recolectaron variables demográficas, causas y grado de compromiso de la función valvular.

**Resultados:** Se incluyeron 3020 pacientes (51,2 % de sexo masculino), con una edad media de 58,2 ± 16,8 años. En el 61,7 %, se observó algún grado de alteración valvular; en el 9,5%, al menos, una valvulopatía de grado significativo (moderado o mayor) y en el 1,7% valvulopatías significativas combinadas. El 4 % de la población presentó estenosis aórtica significativa, que fue la valvulopatía significativa más frecuente, seguida por la insuficiencia mitral (2,9 %) y la insuficiencia tricuspídea (2,3 %). La etiología degenerativa fue la causa más frecuente de disfunción valvular aórtica y mitral, y la causa funcional la principal de insuficiencia tricuspídea significativa. Las valvulopatías significativas aumentaron significativamente con la edad, y afectaron al 23,5 % de los mayores de 75 años. La estenosis mitral y la insuficiencia tricuspídea fueron más frecuentes en pacientes de sexo femenino, sin encontrarse diferencias de género en las valvulopatías aórticas y la insuficiencia mitral.

**Conclusiones:** Las enfermedades valvulares fueron un hallazgo frecuente en nuestra población. Su prevalencia aumentó con la edad; la etiología degenerativa fue la principal causa de compromiso valvular aórtico y mitral, y la funcional de la insuficiencia tricuspídea. La estenosis mitral y la insuficiencia tricuspídea tuvieron diferencias de acuerdo al sexo. Nuestro trabajo aporta información importante y novedosa sobre la epidemiología de las valvulopatías en Argentina.

**Palabras claves:** Enfermedades de las válvulas cardíacas - Epidemiología - Ecocardiografía - Argentina

REV ARGENT CARDIOL 2021;89:290-297. <http://dx.doi.org/10.7775/rac.v89.i4.10418>

Received: 03-26-2021 - Accepted: 06-10-2021

Address for reprints: Juan Benger - E-mail: [registroargenval@gmail.com](mailto:registroargenval@gmail.com), Azcuénaga 980 - C1115AAD - Buenos Aires, Argentina. +54-11- 4961-6027

On behalf of the ARGENVAL Registry Study Group:

<sup>1</sup> Dr. Oscar Orías' Council on Echocardiography and Vascular Doppler Research Group of the Argentine Society of Cardiology, Buenos Aires, Argentina César A. Cado, Miguel S. Ayón, Ariel K. Saad, Javier F. Ventrici, Gerardo C. Filippa, Daniela Sevilla, Matías Failo, Victoria Gallego, Carlos F. Manganiello, Sabrina Sciolini, Guillermo López Soutric, Juan Moukarzel, Federico Dubini, Juan Benger, Iván Constantin, María C. Carrero, Silvia Makhoul, Sergio Baratta, Federico Cintora y Rodrigo Bagnati.

## Abbreviations

<b>ARGENVAL</b>	Argentine Registry of Valvular Heart Diseases	<b>MS</b>	Mitral stenosis
<b>AS</b>	Aortic stenosis	<b>MR</b>	Mitral regurgitation
<b>AR</b>	Aortic regurgitation	<b>RF</b>	Rheumatic fever
<b>EHS</b>	Euro Heart Survey	<b>TR</b>	Tricuspid regurgitation
<b>SD</b>	Standard deviation		

## INTRODUCTION

Valvular heart disease is a highly prevalent disease, affecting 2.5% of the general population in the United States and up to one in eight people over 75 years of age. (1) Taking into account that projections predict population aging, the burden of valvular heart disease is likely to increase with life expectancy. (1, 2) Morbidity and mortality associated with valve disease is considerable and it is estimated that between 10% and 30% of cardiac surgeries are due to valvular surgeries. (3, 4)

Aortic stenosis (AS) and mitral regurgitation (MR) are the most common valvular heart diseases in the United States and Europe. (1, 5) In the Euro Heart Survey (EHS), AS accounted for 43% and MR for 32% of isolated heart valve disease. Multiple valve involvement (20% of patients) was also a common finding. The most common cause of valve disease was degenerative (63%) in all regions of Europe, while rheumatic disease was second, with 22% of patients affected. However, in developing countries, rheumatic fever (RF) continues to be the main cause. (6-9)

In our country, we do not have data regarding the prevalence or etiology of valvular heart diseases. The analysis of this public health problem is of great importance to allocate the appropriate resources to improve its diagnosis and treatment. However, its study is very difficult, since it is a chronic and frequently asymptomatic pathology, and to evaluate its prevalence in the general population, a research should be carried out in a representative sample, which would entail a considerable economic and logistical cost. (10)

The Argentine Registry of Valvular Heart Diseases (ARGENVAL) was designed to know the prevalence of valvular heart diseases in patients who attend echocardiography laboratories in our country on an outpatient basis and the etiologies that most frequently compromise valvular function in our population, as well as the influence of demographic factors on valvular pathologies.

## METHODS

### Study design

ARGENVAL was a retrospective, observational and multi-center registry, originated in the Council on Echocardiography and Vascular Doppler of the Argentine Society of Cardiology. The study was developed between April 2019 and January 2020 and echocardiography laboratories from all over the Argentine Republic were invited to participate. The participating centers had to meet certain standards to ensure the quality of the studies, such as being performed by university cardiologists specialized in echocardiography and pre-

senting the minimum structural and logistical requirements to carry out the registry. Valvular heart function assessment and etiology in cases presenting abnormalities were defined at the discretion of the operator. The data obtained was uploaded through the SurveyMonkey web platform.

### Population

Each center was asked to consecutively include the last 200 patients over 18 years of age who underwent an outpatient transthoracic echocardiogram. Patients who had undergone a study while hospitalized or in the emergency room, who had a history of heart valve surgery or had a poor ultrasound window, were excluded from the study. In each case, demographic variables and echocardiogram results were collected.

### Statistical analysis

Continuous variables with normal distribution were expressed as mean and standard deviation (SD) and those with non-normal distribution, as median with interquartile range 25% -75%. Student's t test or the Wilcoxon rank sum test, as appropriate, was used for the statistical analysis of continuous variables. Discrete variables were expressed as percentages and comparisons were made with the chi-square test with Yates correction or Fisher's exact test, as appropriate. The ratio of affected patients with respect to those examined was calculated to estimate the frequencies of the different valvular heart diseases according to age, gender, geographical distribution and complexity of the institution. The complexity of the center was determined according to hospitalization availability with the possibility of performing endovascular procedures or cardiovascular surgery, hospitalization without availability of valvular procedures and, finally, exclusively outpatient care centers. STATA 12 software was used for the statistical analysis.

### Ethical considerations

The registry was approved by the Bioethics Committee of the Argentine Society of Cardiology. The need for an informed consent was waived as it was an observational and retrospective registry. Nonetheless, the confidentiality of personal data was ensured.

## RESULTS

### Population and participating centers

Among a total of 3020 patients included from the 18 centers in Argentina that participated in the registry (Table 1), 51.6% were male patients and mean age was 58.2 years. The inclusion rate was 100% in 11 centers and greater than 75% in another 2. Most of the centers had a source of private funding and with hospitalization availability. Center complexity included 72% with hemodynamic service, and among these, 92% performed percutaneous aortic valve implantation; 55% had cardiovascular surgery and valvular heart disease outpatient clinic, and 67% had a Heart Team.

	Centers (n=20)	Patients (n=3020)
<b>Patients</b>		
Age (mean and SD)		58.2 (16.8)
Sex		
Female		1462 (48.4%)
Male		1158 (51.6%)
<b>Center distribution</b>		
CABA	7	1104 (36.55%)
Buenos Aires Province		
Inland	5	885 (29.3%)
Greater Buenos Aires	3	539 (17.85%)
Catamarca	2	417 (13.81%)
Tierra del Fuego	1	75 (2.48%)
<b>Center characteristics</b>		
Financing		
Public	3	483 (16%)
Private	15	2537 (84%)
Hospitalization availability	15	2583 (85.5%)
Ambulatory carer	3	437 (14.5%)
<b>Center complexity</b>		
Hemodynamics availability		
TAVI implantation	13	2217 (73%)
Cardiovascular surgery availability	12	2143 (71%)
Heart valve disease outpatient clinic	10	1792 (59.3%)
Heart team availability	10	1641 (54.3%)
	12	1840 (60.9%)

SD: Standard deviation. TAVI: Transcatheter aortic valve implantation

**Table 1.** Characteristics of the patients and participating centers

### Absence of valvular heart disease, significant isolated and combined valve disease

No valvular abnormality was observed in 38.3% of the patients, whose mean age was significantly lower than in those with some lesion (52 vs 62.1 years;  $p < 0.01$ ). In 9.5% of cases the population presented at least one significant heart valve disease, either moderate or severe, with a similar distribution between both genders ( $p=0.65$ ) and a considerably older mean age compared with those without significant valvular lesions (69.2 vs. 56.7 years,  $p < 0.01$ ). Figure 1 shows the distribution of significant valvular heart diseases according to age and gender.

Significant combined valve disease was present in 1.7% of patients, which is equivalent to 18.4% of those who had some significant heart valve disease, and the most frequent combination was mitral regurgitation (MR) + tricuspid regurgitation (TR) (Figure 2). Patients' mean age was 70.3 years, with no significant differences compared with patients with significant isolated heart valve disease ( $p=0.57$ ). Neither were significant differences found according to gender ( $p=0.13$ ). In 0.46% of patients, 3 or more combined significant valve diseases were observed.

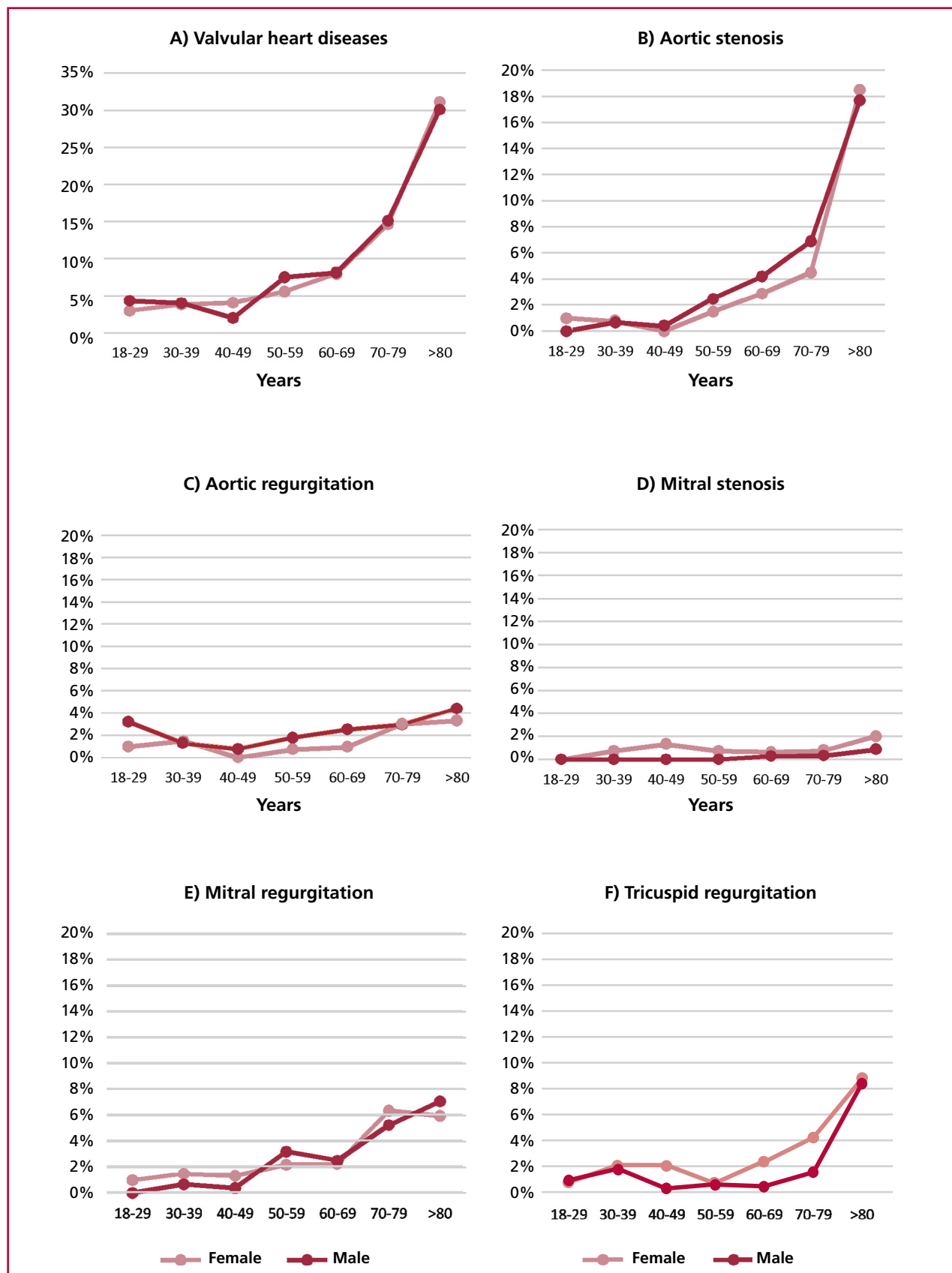
### Aortic valve

**Bicuspid aortic valve:** This type of valve disease was observed in 2.4% of patients, in a population

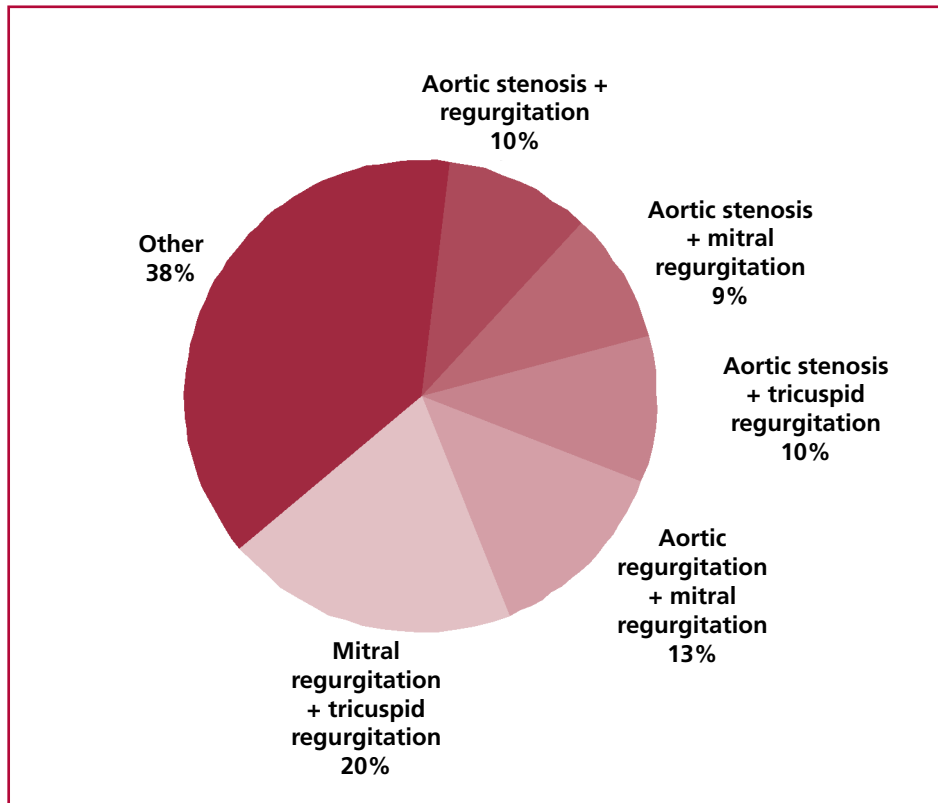
which was significantly younger (51.5 vs. 58.3 years,  $p < 0.01$ ). Moreover, despite being more frequent in male patients (61.1%), the difference did not reach statistical significance ( $p = 0.12$ ).

**Aortic stenosis:** In 7.7% of cases the population presented some degree of AS and in 4% this was at least moderate, resulting in the most frequent and significant valvular heart disease (Table 2). The main etiology was degenerative (86.3%), followed by bicuspid valve disease (9%). This ratio was maintained regardless of the degree of valvular involvement (Figure 3). Mean age of patients with significant AS was higher than in the rest of the population (73.5 vs. 57.5 years,  $p < 0.01$ ) and no significant differences were found according to gender.

**Aortic regurgitation:** This type of valve disease was observed in 21.4% of patients (Table 2), and the most frequent cause was degenerative (59.6%), followed by aortic dilation (8.7%) and bicuspid valve disease (5.9%) (Figure 3). Significant aortic regurgitation (AR) was observed in 1.9% of the population and the mean age of these patients was 64.7 years, significantly older than the rest of the population (58 years),  $p < 0.01$ . The most frequent cause of significant AR was degenerative in almost half of the cases. Although it was more prevalent in males (62.5), the difference was not significant ( $p=0.09$ ).



**Fig. 1.** Percentage of significant valvular heart disease according to patient age and gender for: A) presence of any significant valve disease, B) significant aortic stenosis, C) significant aortic regurgitation, D) significant mitral stenosis, E) significant mitral regurgitation and F) significant tricuspid regurgitation.



**Fig. 2.** Presentation of combined significant valvular heart diseases.

**Table 2.** Frequency of individual valve disease in the population.

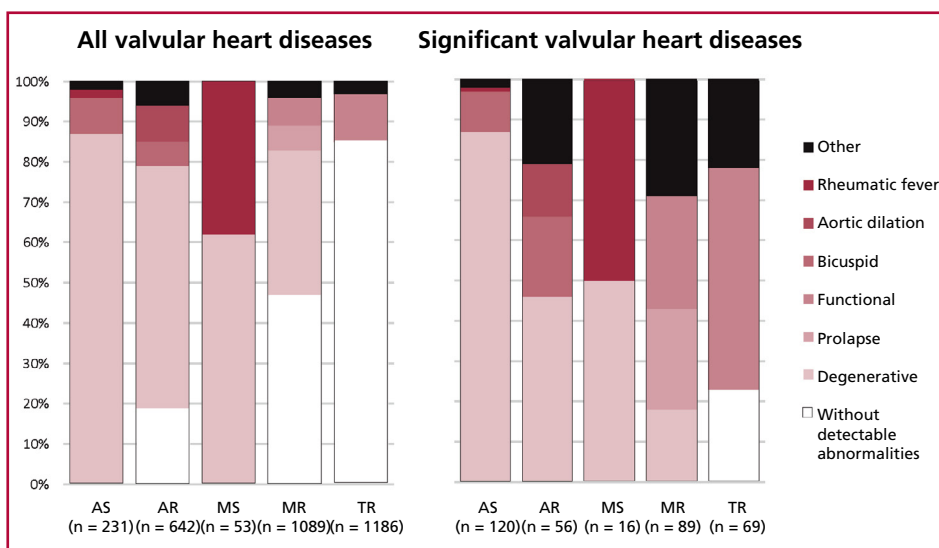
	Aortic Valve		Mitral Valve		Pulmonary Valve		Tricuspid Valve	
	Stenosis n (%)	Regurgitation n (%)	Stenosis n (%)	Regurgitation n (%)	Stenosis n (%)	Regurgitation n (%)	Stenosis n (%)	Regurgitation n (%)
Without valve disease	2787 (92.3%)	2374 (78.6%)	2966 (98.2%)	1893 (62.7%)	2727 (90.3%)	2374 (78.6%)	3018 (99.9%)	1771 (58.6%)
With non-significant valve disease	113 (3.7%)	590 (19.5%)	38 (1.3%)	1038 (34.4%)	285 (9.4%)	590 (19.5%)	1 (0.1%)	1180 (39.1%)
With significant valve disease	120 (4%)	56 (1.9%)	16 (0.5%)	89 (2.9%)	8 (0.3%)	56 (1.9%)	1 (0.1%)	69 (2.3%)
Moderate valve disease	73 (2.4%)	48 (1.6%)	12 (0.4%)	68 (2.2%)	8 (0.3%)	48 (1.6%)	1 (0.1%)	52 (1.7%)
Severe valve disease	47 (1.6%)	8 (0.3%)	4 (0.1%)	21 (0.7%)	0 (0.3%)	8 (0.3%)	0 (0.1%)	17 (0.6%)

**Mitral stenosis:** It was a rare valve disease, and only 0.5% had significant mitral stenosis (MS) (Table 2) and the most prevalent cause was degenerative (62.3%), while the rest (37.7%) was secondary to RF. Patients with significant MS were more frequently women (81.3 vs. 18.7%,  $p < 0.01$ ) and the etiology was 50% degenerative and 50% RF. Mean age was 65.1 years, without significant differences with respect to the rest of the population (58.1 years,  $p = 0.09$ ).

**Mitral regurgitation:** In 37.3% of cases, patients had some degree of MR and 2.9% had at least

moderate MR, resulting in the second most frequent significant heart valve disease (Table 2). In 45.5% of cases, no valvular abnormalities were observed to justify valvular heart disease. Of the identifiable causes, the most frequent was fibrosis and calcification of the valve and the annulus, followed by prolapse (Figure 3). Mean age of significant MR was notably older than in the rest of the population (68.6 vs. 57.8 years,  $p < 0.01$ ). Mitral regurgitation was similarly distributed between both genders ( $p = 0.68$ ) and functional causes were the most frequent (overall 28.1%, ischemic

**Fig. 3.** Etiology of valvular heart disease, on the left taking into account all cases and on the right only significant valve diseases.



AS: aortic stenosis, AR: aortic regurgitation, MS: mitral stenosis, MR: mitral regurgitation, TR: tricuspid regurgitation.

16.9% and non-ischemic 11.2%), followed by prolapse, valve fibrosis and calcification.

#### Pulmonary valve

**Pulmonary stenosis:** This was a very rare valve disease (Table 2).

**Pulmonary regurgitation:** In 9.7% of cases patients presented some degree of regurgitation and only 0.3% had significant regurgitation (Table 2). No abnormalities that justified valve disease were detected in 93.9% of the patients, and pulmonary hypertension and prolapse were the main defects detected.

#### Tricuspid valve

**Tricuspid stenosis:** Only 2 cases of tricuspid stenosis were observed (Table 2).

**Tricuspid regurgitation:** Its prevalence was 41.4%, making it the most frequent valvular heart disease (Table 2). The main identifiable cause was functional followed by secondary to endocavitary catheter placement. In more than 80% of cases, no valvular, ventricular or atrial ultrasound abnormalities were observed that explained the tricuspid reflux (Figure 3). In 2.3% of the patients, TR was at least moderate, and it was classified as the third most frequent significant valvular heart disease (Table 2). The most common cause of significant TR was functional, which was observed in more than half of the patients. In 56% of the cases, significant TR was isolated, and it was associated with left valve disease in the remaining 44%. Mean age of patients with significant TR was greater than that of the rest of the population (69 vs. 57.9 years,  $p < 0.01$ ) and its presence was more frequent in women (65.2%,  $p < 0.01$ ).

#### Valvular heart disease and centers

The centers located in the Autonomous City of Buenos Aires had a considerably higher proportion of patients

with significant valvular heart disease than those in the provinces and Greater Buenos Aires (14.7% vs. 7.5% vs. 4.1%, respectively,  $p < 0.01$  for the comparison between each of them). Similarly, public funding institutions had a higher proportion of significant valvular heart disease (23.2 vs. 6.9%,  $p < 0.01$ ). Regarding the complexity of the center, those with hospitalization and the possibility of performing valvular procedures had an appreciably higher proportion of patients with significant heart valve disease (11.1%) than those with hospitalization and without the possibility of performing hemodynamics or surgical procedures (9.3%) or with exclusively ambulatory care (5.1%;  $p < 0.01$ ).

#### DISCUSSION

To our knowledge, ARGENVAL is the first registry that shows data on the prevalence and etiology of valvular heart disease in the Argentine population. The registry showed that valve diseases are frequently observed in patients who attend echocardiography laboratories on an outpatient basis in our country, since 6 out of 10 studies present some degree of valvular heart disease and in almost 1 out of 10 a significant valve disease is present. The prevalence found was higher than that observed in community and population registries, where significant heart valve disease was found in 2.5% to 6.4% of their population. (1, 11) This finding was predictable due to the type of study design, which included patients referred for evaluation and, therefore, sicker and older than the general population. Nevertheless, this information is of great importance to assess the magnitude of the problem in Argentina.

In previous studies, AS and MR were the most frequently found significant valvular heart diseases; AS was most common in Europe and MR in the United States. (1, 5, 11-13) We also found AS and MR as the

main significant valve diseases, since they represented 41.6% and 30.9%, respectively. Similarly, combined heart valve diseases had a very comparable proportion to that of the EHS, affecting about 20% of patients. (5, 12) With respect to right valve pathologies, in the main registries in which they were evaluated their frequency was, generally far inferior to mitral and aortic valve disease. (5, 12-14) In contrast to those results, our work showed TR as a very common disease, since it was the most frequent valve disease and the third when taking into account only those of significant degree. In the recent OxVALVE population study, the prevalence of significant TR was very similar to ours (2.7% vs. 2.3%). (11) Although these findings could be due to demographic and ethnic differences between the populations evaluated, the tendency in recent years to recognize the problems associated with the traditionally so called "forgotten valve" may have some role in this scenario.

Consistent with other community and population registries, we observed that the prevalence of valvular heart diseases increases markedly with age, significantly affecting 23.5% of patients over 75 years of age in our population. (1, 5, 11, 13, 15) This phenomenon coincides with the change in epidemiology observed in the United States and Europe, in which a degenerative etiology is the first cause of valve disease and RF is an infrequent finding. In our study, the degenerative cause was the most frequent of aortic and mitral valve pathologies, representing 86% of AS, 60% of AR, 62% of MS, and 36% of MR. Only 21 patients presented valve disease due to RF, all with mitral involvement and, in some cases, with multiple valvular heart disease, which also confirmed the decrease of this problem in our country. In the case of the tricuspid valve, the main mechanism of TR was, by far, functional. Although this mechanism was also a frequent finding in the EHS, its presentation was observed especially associated with left valve disease, which was found in more than 90% of TR. (16) On the other hand, in our study, TR presented in isolation in 56% of cases, so the functional origin maintained a similar proportion to that previously described. Again, perhaps demographic, ethnic disparities, or associations with other known, unexamined conditions, such as atrial fibrillation, might explain these differences.

Finally, several studies have described differences in the prevalence of some types of valvular heart disease according to gender. Thus, aortic valve disease has been more frequently found in male patients and TR in female patients. (1, 11, 14, 17) In our case, the only valve diseases that had a significant association with gender were MS and TR, which were more commonly found in women. Aortic regurgitation, despite not having reached statistical significance, showed a trend towards a higher frequency in men.

The registry has limitations. Firstly, the study design was not population-based, but included referred patients and, therefore, the prevalence of disease does

not represent that of the general population. Secondly, as there was no central laboratory available to review the studies carried out, there may be discrepancies in the classification between different operators and centers. Nonetheless, the centers had to comply with quality standards for their participation, so this limitation probably did not have great significance. Thirdly, given the retrospective nature of the registry, data not included in the study report could not be retrieved, as for example mechanisms of valve lesions or quantification of the degree of involvement. However, this type of design allowed us to obtain a number of centers and enrolled patients that would have been impossible had it been a prospective study. Finally, although it was a national registry and efforts were made to recruit centers from all over the country, most of the centers were from the Autonomous City of Buenos Aires and the Province of Buenos Aires. When we compared the frequency of valvular heart disease among the centers in the rest of the provinces, there were no significant differences according to their location, but it cannot be assured that other sites are represented by this registry.

## CONCLUSIONS

Valvular heart disease was a frequent finding, its prevalence increased with age and, with the exception of MS and TR, it was similarly distributed between both sexes. Aortic stenosis was the most frequent significant valve disease, followed by MR and TR. The main cause of aortic and mitral valve stenosis and regurgitation was degenerative, and functional in the case of TR. The centers located in the Autonomous City of Buenos Aires, with public funding and of greater complexity, presented a higher prevalence of significant valvular heart disease.

## Conflicts of interest

None declared.

(See authors' conflicts of interest forms on the website/ Supplementary material)

## Acknowledgements

We thank the ARGENVAL Registry researchers for their selfless and voluntary commitment to the development of quality, independent scientific material in Argentina. To our families, for understanding that being an independent researcher in Argentina implies work and dedication without remuneration other than the satisfaction of the work achieved.

## REFERENCES

1. Nkomo VT, Gardin JM, Skelton TN, Gottdiener JS, Scott CG, Enriquez-Sarano M. Burden of valvular heart diseases: a population-based study. *Lancet* 2006;368:1005-11. [https://doi.org/10.1016/S0140-6736\(06\)69208-8](https://doi.org/10.1016/S0140-6736(06)69208-8)
2. US Census Bureau. United States Census 2000. Washington, DC, USA: US Census Bureau, 2001.
3. Mahmood KT, Anees M, Asghar A. Valvular heart diseases - a re-

view. *J Biomed Sci Res* 2011;3:315-21.

4. Sheikh AM, Livesey SA. Surgical management of valve disease in the early 21st century. *Clin Med* 2010;10:177-81. <https://doi.org/10.7861/clinmedicine.10-2-177>
5. Iung B, Baron G, Butchart EG, Delahaye F, Gohlke-Bärwolf C, Levang OW, et al. A prospective survey of patients with valvular heart disease in Europe: The Euro Heart Survey on Valvular Heart Disease. *Eur Heart J* 2003;24:1231-43. [https://doi.org/10.1016/S0195-668X\(03\)00201-X](https://doi.org/10.1016/S0195-668X(03)00201-X)
6. Demirbağ R, Sade LE, Aydın M, Bozkurt A, Acartürk E. The Turkish registry of heart valve disease. *Turk Kardiyol Dern Ars* 2013;41:1-10. <https://doi.org/10.5543/tkda.2013.71430>
7. Watkins DA, Johnson CO, Colquhoun SM, Karthikeyan G, Beaton A, Bukhman G, et al. Global, Regional, and National Burden of Rheumatic Heart Disease, 1990-2015. *N Engl J Med* 2017;377:713-22. <https://doi.org/10.1056/NEJMoa1603693>
8. Ordunez P, Martínez R, Soliz P, Giraldo G, Mujica OJ, Nordet P. Rheumatic heart disease burden, trends, and inequalities in the Americas, 1990-2017: a population-based study. *Lancet Glob Health* 2019;7:e1388-97. [https://doi.org/10.1016/S2214-109X\(19\)30360-2](https://doi.org/10.1016/S2214-109X(19)30360-2)
9. Pradegan N, León-Wyss JR, Iribarren JR, García E, Roa W, Corniel P, et al. Contemporary trends in surgical rheumatic valve disease in a Caribbean nation. *Int J Cardiol* 2020;328:215-217. <https://doi.org/10.1016/j.ijcard.2020.12.023>
10. Iung B, Vahanian A. Epidemiology of valvular heart disease in the adult. *Nat Rev Cardiol* 2011;8:162-72. <https://doi.org/10.1038/nrcardio.2010.202>
11. D'Arcy JL, Coffey S, Loudon MA, Kennedy A, Pearson-Stuttard J, Birks J, et al. Large-scale community echocardiographic screening reveals a major burden of undiagnosed valvular heart disease in older people: the OxVALVE Population Cohort Study. *Eur Heart J* 2016;37:3515-22. <https://doi.org/10.1093/eurheartj/ehw229>
12. Iung B, Delgado V, Rosenhek R, Price S, Prendergast B, Wendler O, et al; EORP VHD II Investigators. Contemporary Presentation and Management of Valvular Heart Disease: The EURObservational Research Programme Valvular Heart Disease II Survey. *Circulation* 2019;140:1156-69. <https://doi.org/10.1161/CIRCULATIONAHA.119.041080>
13. Andell P, Li X, Martinsson A, Andersson C, Stagmo M, Zöller B, et al. Epidemiology of valvular heart disease in a Swedish nationwide hospital-based register study. *Heart* 2017;103:1696-703. <https://doi.org/10.1136/heartjnl-2016-310894>
14. Singh JP, Evans JC, Levy D, Larson MG, Freed LA, Fuller DL, et al. Prevalence and clinical determinants of mitral, tricuspid, and aortic regurgitation (The Framingham Heart Study). *Am J Cardiol* 1999;83:897-902. [https://doi.org/10.1016/S0002-9149\(98\)01064-9](https://doi.org/10.1016/S0002-9149(98)01064-9)
15. Eweborn GW, Schirmer H, Heggelund G, Lunde P, Rasmussen K. The evolving epidemiology of valvular aortic stenosis. the Tromsø study. *Heart* 2013;99:396-400. [https://doi.org/10.1016/S0002-9149\(98\)01064-9](https://doi.org/10.1016/S0002-9149(98)01064-9)
16. Iung B, Baron G, Tornos P, Gohlke-Barwolf C, Butchart EG, Vahanian A. Valvular heart disease in the community: a European experience. *Curr Probl Cardiol* 2007;32:609-61. <https://doi.org/10.1016/j.cpcardiol.2007.07.002>
17. Reid CL, Anton-Culver H, Yunis C, Gardin JM. Prevalence and clinical correlates of isolated mitral, isolated aortic regurgitation, and both in adults aged 21 to 35 years (from the CARDIA study). *Am J Cardiol* 2007;99:830-4. <https://doi.org/10.1016/j.amjcard.2006.10.048>