CARDIOLOGIE
TUNISIENNE

Epidemiologic spectrum of severe valvular heart disease in Sfax: about 589 cases

Le profil épidémiologique des valvulopathies sévères à Sfax: à propos de 589 cas

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Résumé

Introduction: les valvulopathies représentent un véritable problème de santé dans les pays en voie de développement. Le but de cette étude était de déterminer la fréquence, le profil épidémiologique, les signes cliniques et la gestion de valvulopathies sévères dans un centre tertiaire de cardiologie en Tunisie. Méthodes: Entre Janvier 2010 et décembre 2013, 589 adultes avec valvulopathies sévères ont été inclus dans cette étude rétrospective. Toutes les caractéristiques démographiques et échocardiographiques ainsi que les stratégies thérapeutiques ont été étudiées.
Résultats: l'âge moyen était de 55 ans. Parmi les 589 patients, 360 (61.1 %) étaient des femmes. En général la valve mitrale était la valve la plus touchée (55.8 %) et la rétrécissement mitral était la valvulopathie la plus fréquente (30.4 %). Le rhumatisme articulaire aigu (RAA) était l'étiologie la plus fréquente soit chez 355 patients (60.3 %). Le traitement chirurgical a été indiqué dans 64.1 % de tous les patients. Seulement 36.1 % des cas ont bénéficié d'une chirurgie de remplacement valvulaire. Une dilatation mitrale percutanée a été réalisée dans 36 % des cas. Les complications post-opératoires ont été notées chez 39 patients (24.2 %). La mortalité a été notée chez 22 patients (13.6 %). Il n'y avait aucune corrélation significative entre l'âge, la valve remplacée et l'incidence de mortalité post-opératoire.
Conclusion: Les valvulopathies restent un problème de santé publique en Tunisie et elles sont fréquemment sévères. Le RAA était l'étiologie la plus commune. Les valvulopathies sévères sont associés à une lourde mortalité et morbidité post opératoire. Des études multicentriques pourraient nous aider à mieux étudier ces valvulopathies dans notre pays.

Summary

Background: Valvular heart disease (VHD) is a significant and an increasing health problem in the developing world. The aim of this study was to determine the prevalence, the epidemiological profile, the clinical feature and the management of the severe VHD in a single cardiovascular tertiary centre of Tunisia. Methods: From January 2010 to December 2013, 589 adult cases with severe VHD were included in this retrospective study. All the required demographic and echocardiographic characteristics and the treatment strategies were studied.
Results: The mean age was 55 (17.39) years. Out of the 589 patients, 360 (61.1%) were females. Overall, the mitral valve was the most common involved valve (55.8%) and 30.4% patients with severe VHD had mitral stenosis (MS) alone. Rheumatic heart disease (RHD) was the most common etiology present in 355 (60.3%) patients. Surgical treatment was indicated in 64.1% of all patients. Among total, only 36.1% of the cases underwent valve replacement surgery. Percutaneous mitral balloon commissurotomy was performed in only 36% of the patients with severe MS. Early postoperative complications were occurred in 39 (24.2%) patients. Mortality was occurred in 22 (13.6%) patients. There were no significant correlations between age, simultaneous valve repair and replacement, and the incidence of postoperative mortality.
Conclusion: VHD remains public health problem in Tunisia and is frequently severe. RHD was the most common etiology of severe VHD. Severe VHD was associated to high early postoperative morbidity and mortality. Multicenter collaborative studies will help to better describe the pattern of VHD.

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Valvular heart diseases (VHD) are still a major cause of significant morbidity and mortality in developing countries especially in Africa where the epidemiologic factors are still prevalent (1). The spectrum of VHD varies in different regions of the world and there have been significant changes in the epidemiology of VHD in the past decades. In developing countries, the rheumatic heart disease (RHD) remains the most common cause of VHD. Its prevalence is high, between 20 and 30 cases per 1000 subjects (2).

The objective of this study was to determine the prevalence, the epidemiological profile, the clinical feature and the management of the severe VHD in a single cardiovascular tertiary centre of Tunisia.

PATIENTS AND METHODS

The present retrospective study was conducted in the department of cardiology of Hedi Chaker University hospital, a major cardiac referral centre in Tunisia. The hospital receives referrals from other health institutions for the investigation and/or management of suspected heart disease. All the data over a 4-year period from January 2010 to December 2013 were reviewed. Baseline characteristics, etiology and therapeutic strategies were collected from electronic medical records. The patients presenting severe VHD according to the criteria of the European Association of Echocardiography and the American Society of Echocardiography were included (3,4). The RHD was diagnosed on the basis of the history of rheumatic fever and the echocardiographic criteria defined according to the world heart federation by the presence of any definite evidence of valve regurgitation or stenosis, and at least two morphologic abnormalities, such as restricted leaflet mobility, focal or generalized valvular thickening, and abnormal subvalvular thickening of the affected valve (5). The diagnosis of degenerative VHD was based on echocardiographic findings. The ischemic VHD was diagnosed according to the history of ischemic heart disease. All patients who underwent surgery were followed-up at 30-days.

Statistical analysis

The data collected was analysed using SPSS version 18 for windows. Descriptive statistics including means, standard deviations (SD), and frequencies were generated.

Means of continuous variables were compared using student's t-test and the analysis of variance (ANOVA de Welch) among the groups while proportions were compared using the Chi-square test. A P value of <0.05 was considered as statistically significant.

RESULTS

A total of 24422 echocardiographic examinations were performed over the 4-year period of the study. There were 959 patients with a significant VHD as defined by the criteria of "the European Heart Survey (EHS) on valvular heart disease" (6), with 589 (61.4%) patients having a definite severe VHD. Out of the 589 patients with severe VHD, 360 (61.1%) were females. The patients presenting severe VHD were significantly older compared to those with non-severe VHD (mean (SD) = 55 (17.39) versus 51 (15.15) years, p<0,001).The mean age was lower in patients with mitral stenosis (MS) (49.15 (13.84) years) and aortic regurgitation (AR) (46.41 (19.53) years) than in aortic stenosis (AS) and mitral regurgitation (MR) (69.2 and 61.4 years respectively), (all p < 0.001). The female gender was predominant in MS and AR.

Severe VHD was the first presentation of the VHD in 174 (29.5%) patients. The most common clinical indication and referral for echocardiography was dyspnea (58%) and the presence of a heart murmur on clinical examination (25.9%).At diagnosis, 335 (56.8%) patients were at New York Heart Association (NYHA) functional class II. The demographic and clinical features for the study population are summarized in table 1.

Table 1: Clinical characteristics of the patients with severe VHD

	All cases	
	N (Total = 589)	%
Age (years, SD)	55 (17.39)	
Gender, female	360	61.1
Functional capacity		
NYHA I	130	22
NYHA II	335	56.8
NYHA III	93	15.8
NYHA IV	31	5.2
Comorbid risk factors		
Hypertension	94	16
Diabetes	56	9.5
Smoking	168	28.5
CKD	64	10.8

Overall, the mitral valve was the most common involved in severe VHD, accounting for 55.8% of all cases. One hundred and seventy nine (30.4%) patients with severe VHD had MS alone **(Figure 1)**. The most common etiology of severe VHD was RHD present in 355 (60.3%) patients followed by the degenerative cause in 144 (24.4%) patients. The most common echocardiographic diagnosis was rheumatic pure MS present in 179 (30.4%) patients.

The rheumatic disease mainly affected the mitral valve **(Figure 2)**.
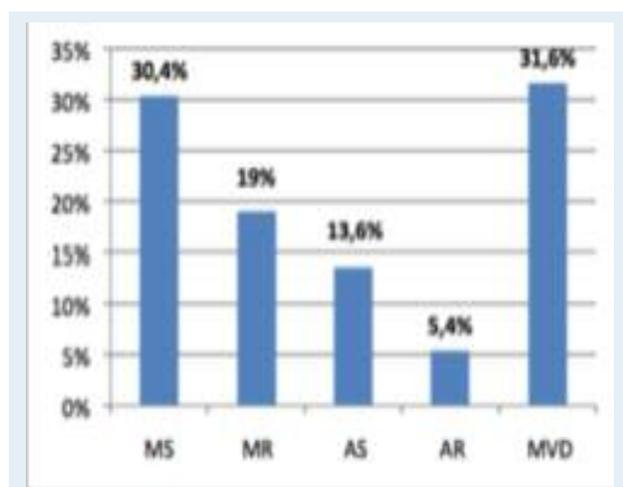
Figure 1 : Different severe VHD involvement in the study population

AS: aortic stenosis; AR: aortic stenosis; MS: mitral stenosis; MR: mitral regurgitation; MVD: multiple valve disease
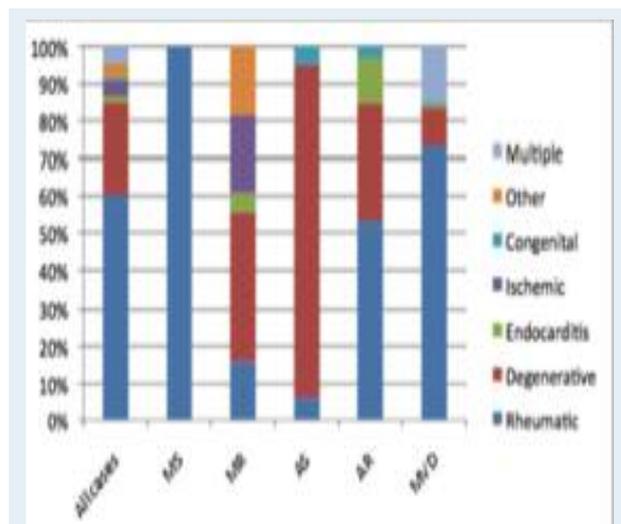
Figure 2 : Different etiologies according to the valve involvement in the study population

AS: aortic stenosis; AR: aortic stenosis; MS: mitral stenosis; MR: mitral regurgitation; MVD: multiple valve disease

Among patients with severe VHD, either surgical or percutaneous treatment was indicated for 446 (75.72%) patients. Only 161 (36.1%) patients were finally operated. The others were lost to follow-up or refused the surgical treatment. Almost the quarter of the patients presenting single VHD underwent valve surgery. Sixty-six (36.8%) patients with isolated MS were treated

by percutaneous mitral balloon commissurotomy (PMBC). While PMBC was indicated in MS, prosthetic valve replacement was the main treatment selected in the other VHDs. Mitral valve repair was the suggested treatment in 28.8% of severe isolated MR cases. Bioprosthesis was applied in 12.2% of patients with prosthetic valve replacement. 80% of bioprosthetic valve replacements were in the aortic position. The different types of intervention in patients with single VHD are summarized in Tables 2 and 3. Concomitant surgical intervention was performed in 28 (17.4%) patients. A concomitant aorto coronary bypass grafting was the most performed (46.4%).

Table 2: Surgical or percutaneous treatment of isolated single VHD in the study population

	Suggested treatment	Number of trea- ted patients	%
Mitral stenosis (N = 179)			
PMBC	66	66	100
Surgery			
Mechanical prosthesis	91	36	40,61
Bioprosthesis		1	
Medical treatment	22	22	100
Total	179	125	69.83
Mitral regurgitation (N = 112)			
Valve repair	19	11	57.89
Prosthesis			
Mechanical prosthesis	47	15	36.17
Bioprosthesis		2	
Medical treatment	46	46	100
Total	112	74	66.07
Aortic stenosis (N= 80)			
Surgery			
Mechanical prosthesis	78	11	25.67
Bioprosthesis		9	
Medical treatment	2	2	100
Total	80	22	27.5
Aortic regurgitation (N = 32)			
Surgery			
Mechanical prosthesis	32	6	28.12
Bioprosthesis		3	
Total	32	9	28.12

PMBC: percutaneous mitral balloon commissurotomy

Table 3: Management of mixed and multiple VHD in the study population

	Suggested treatment	Number of treated patients	%
PMBC	2	2	100
Surgery	179	70	39,10
Mitral prosthesis	44	19	43,18
Aortic prosthesis	62	13	20,96
Mitral and aortic prosthesis	72	37	51,38
Mitral repair and aortic prosthesis	1	1	100
Medical treatment	5	5	100
Total	186	77	41,39

PMBC: percutaneous mitral balloon commissurotomy

The early major postoperative complications (within 30 days or during the same hospitalization after the operation) occurred in 39 (24.2%) patients. The main complications are summarized in table 4.

Table 4: Early postoperative complications in the study population

	N	% (N/39)	% (N/161)
IE	12	30,76	7,45
Cardiogenic choc	8	20,51	4,96
Acute Heart failure	2	5,12	1,24
Tamponade	2	5,12	1,24
Major bleeding	2	5,12	1,24
Acute kidney failure	2	5,12	1,24
MI	1	2,56	0,62
AVB	1	2,56	0,62
Prosthesis dysfunction	1	2,56	0,62
Others	8	20,51	4,96
Total	39	100	24,22

Major bleeding: Bleeding leading to surgery or intervention, IE: infective endocarditis, MI: myocardial infarction, AVB: auriculo-ventricular block

There were 22 (13.6%) early deaths (within 30 days or during the same hospitalization after the operation) in the group of the patients who underwent valve surgery. There was no statistically significant relation between different clinical and echocardiographic parameters and the early mortality in the study population (Table 5).

Table 4: Early postoperative complications in the study population

Risk factor			Death N	%	p value
Sex	Male	77	8	10,4	0,24
	Female	84	14	16,7	
Age (years)	< 65	126	16	12,7	0,57
	≥ 65	35	6	17,1	
Diabetes	Yes	17	2	11,8	1
	No	144	20	13,9	
CKD	Yes	3	1	33,3	0,35
	No	158	21	13,3	
Functional class (NYHA)	NYHA I	6	2	33,3	0,17
	NYHA II	113	13	11,5	0,11
	NYHA III	26	4	15,4	0,76
	NYHAIV	10	3	30	0,15
Valve involvement	MS	37	5	13,5	0,97
	MR	25	6	24	0,11
	AS	20	0	0	0,07
	AR	9	1	11,1	1
	MVD	70	10	14,28	0,84
Etiology	Rheumatic	89	13	14,6	0,69
	Ischemia	1	0	0	-
	degenerative	52	6	11,5	0,58
	Infective endo-carditis	10	1	10	1
	Others	8	2	25	0,29
SPAP (mmHg)	≥50	47	9	19,1	0,13
	<50	90	9	10	
LVEF (%)	≤50%	37	4	10,8	
	>50%	105	17	16,2	0,42

NYHA: New York Heart Association, CKD: chronic kidney disease, MS: mitral Stenosis, MR: mitral regurgitation, AS: aortic stenosis, AR: aortic regurgitation, MVD: mixed and multiple valve disease, SPAP: systolic pulmonary artery pressure, LVEF: left ventricular rejection fraction

DISCUSSION

In this study covering three years of activities in a major referral cardiovascular unit in Tunisia, we have reported the contemporary pattern of severe VHD in adults.

Rheumatic heart disease remains by far the leading cause of severe valvular disease in our study. It accounted for 60% of severe VHD, followed by degenerative etiologies in 24%. Severe VHD occurred in young people and most often in female.

In fact, in Tunisia as in developing countries, RHD still the major cause of VHD (2). Its prevalence is high, between 20 and 30 cases per 1000 subjects when using systematic echocardiographic screening (2).This high prevalence is due to the sustained incidence of acute rheumatic fever, estimated at between 5 and 50 per 100,000 per year in developing countries (7). The risk factors of acute rheumatic fever and RHD are largely related to socio-economic status, as attested by the influence of malnutrition and overcrowding (8). The preponderance of female young patients with severe VHD in our study is similar to the conventional epidemiological picture of VHD in the developing and emerging countries where the RHD was the most frequent etiology. In a South African center, RHD still accounted for 72% of valvular disease in 2006-2007 (9). At diagnosis, the median age of patients presenting with RHD was 43 years and 68% were female (9).In a recent survey in Turkey that included 1,300 patients hospitalized in 42 centers in 2009, RHD accounted for 46% of all VHD, followed by degenerative etiologies in 29%. The mean age was 57 years and 60% of patients were females 10. This trend is different from the epidemiologic feature in developed countries where the degenerative etiology is the most frequent (11, 12, 13). In a large study performed in the US, which included 11,911 subjects, the prevalence of significant VHD increased with age (14). In the Euro Heart Survey on valvular heart disease, which was performed during a 4-month period in 2001 in 92 centres in 25 European countries, the degenerative etiology was the leading cause of valvular disease, in 63% of patients and in all European regions, followed by RHD in 22% of patients (6). The most common valvular involvement in our patients with severe VHD was the isolated MS (30%), and the multiple VHD (31%). The etiology of MS was exclusively rheumatic. In the South African study, the mitral valve was the most frequently involved. In this study, of the 344 patients presenting with RHD, 59% had MR, 37% AR, 30% MS and 9% AS (9). In the Turkish registry, the MR (43%) and multiple VHD (32%) were the most frequent VHD. The incidence of MS was only 15% (10). The rheumatic etiology may explain the low incidence of MS in industrialized countries. In fact, in the USA, the incidence of MS was 0.1% (14). In the Euro Heart Survey (6), degenerative AS was the most frequent single-valve disease (43%), followed by MR (32%), AR (13%) and MS (12%). In this study, RHD was the cause of MS in 85.4% of patients, and 81% of these patients were women(6).

In our study, the dyspnea was the most common symptom (58%). Almost the half of our patients was at NYHA functional class II and only 130 (22%) patients were asymptomatic. Similarly, in the Turkish registry, 64% of the patients presented NYHA class I – II symptoms (10). The diagnosis of asymptomatic severe VHD is important as it is associated to best prognostic and quality of life. Then, the screening is very important for early diagnosis and prevention especially in RHD.

Among patients with severe VHD, either surgical or percutaneous treatment was indicated for 446 (75.72%) patients. The reasons for not advising surgical intervention in patients with severe VHD were either cardiac, extracardiac, or both. As detailed in previous studies, the reasons for not advising surgery were severe depression of the left ventricular function, recent myocardial infarction, severe coronary disease which is seldom not by passable unless diffuse and distal, presence of multiple comorbidities (6, 15). Actually, according to the guidelines, the percutaneous treatment may be indicated in selected cases of severe VHD after a heart team (16). Unfortunately, trans-catheter aortic valve implantation and mitra-clip were not available in our center.

The characteristics of the patients whom surgical treatment was suggested in our study are similar to those of other series. Prosthetic valve replacement was the most suggested treatment in severe VHD. Bioprosthesis was applied in only 12.2%. 80% of bioprosthetic valve replacements were in the aortic position. In this study as in previous series, the majority of patients with severe AS were operated around the age of 70 years (6, 17, 18). Bioprosthetic valve replacement was preferred in AS patients more than 65 years old (6, 19, 20). In mitral valve disease more conservative techniques are gaining popularity. In the Euro Heart Survey, nearly half of the patients presenting MR underwent mitral valve repair (6). This encouraging figure probably reflects the increasing confidence in the technique due to the accumulation of data showing its good short and long term efficacy. However, in the present study, mitral repair was indicated in 28% of MR and was finally done in only 12%. This difference might be due to the origin of MR and the valve anatomy, which could be not suitable for repair, especially in the RHD. Furthermore, the absence of local expertise in conservative surgery might remain a significant limitation for a larger use of conservative techniques. The PMBC was performed in 37% of severe MS in our study, similarly to the European Heart Survey study (33.9%) (6). In the Turkish Survey, the PMBC was applied in 76% of all cases of MS (10). As reported in the literature, PMBC is preferred in the treatment of rheumatic MS (21). The reasons for the

difference between these findings may be the valve anatomy, the increased incidence of RHD and the different age of the MS study group.

In-hospital morbidity after valve intervention observed in this study was 24.2%. In a previous prospective study conducted by Samiei et al. in Iran, the overall morbidity occurred in 26.6% after valve intervention (22). Overall early postoperative mortality in this study was high around 13.6%. In previous reported studies, this rate varies from 1 to 15% (23). It was higher than the rates reported in the most recent studies and surgical registries such as the Euro Heart Survey, the STS database in the USA and the United Kingdom Cardiac Surgical Register (6, 22 - 27). In this study, there were no significant predictive risk factors for early postoperative mortality. The mortality rate was higher in female and in older patients (> 65 years) but with no significant difference. The anatomic site of the repaired valve and the number of repaired valves were also associated to higher mortality incidence but with no significant difference. This might be due to small study group size. In previous reported studies, there was a statistically significant relation between the incidence of mortality, and the history of comorbidities in the study population (22). The number, the site and the type of prosthetic valve replacement were also associated to higher mortality (28, 29).

Study limitations
Our study is a hospital based retrospective analysis hence subject to bias. Patients diagnosed with severe VHD may be those with symptomatic disease hence more likely to seek medical attention. The limited number of patients may present another limitation. Thus, our results may not reflect the true burden of severe VHD in the general population. National multicenter epidemiological data are needed to confirm these findings.

CONCLUSION

Severe VHD remains a major healthcare problem in our country. Rheumatic fever is still the most common etiology of VHD in our patients. There should be a renewed focus on RHD prevention. Multicenter collaborative studies will help to better describe the pattern of VHD and guide in health policy.

Disclosures: none

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