A Multi-Center Study of the Pathologies of Valvular Heart Diseases: 
5 year Analysis of More Than 3400 Patients in Iran

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Abstract

Background: The purpose of this study is to provide insight into pathology patterns of cardiac valves, which remains a major cause of mortality and morbidity in Iran as a developing country.

Methods: This prospective study included 3418 consecutive cardiac surgery patients who underwent valve surgery over the past 5 years in 6 major hospitals. Etiologic and pathologic data of the valves were based on either pathologic reports (for replaced valves) or gross detection of the surgeons (for repaired valves).

Results: The mean age of subjects was 43.98±14.45 years. 1616(47.27%) of them were male and 1802(52.73%) were female. Approximately 46% (1572) of the patients underwent mitral valve surgery. Mitral valve disease was found to be due to ischemia in 327(9.56%), infective endocarditis in 68 (1.99%), congenital problems in 71(2.08%) and degenerative etiology in 264(7.72%). Rheumatic valve disease was most frequent in patients of 40-49 years old.

Conclusions: This study shows that rheumatic valvular disease remains the most frequent valvular pathology among patients undergoing valvular surgery in Iran. The relatively high mean age of patients with rheumatic valvular disease emphasizes the priority of this health problem in Iran which requires particular attention, especially in terms of prevention and also treatment.

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Introduction

Outstanding promotions during the past 3 decades took place in diagnostic devices and treatment procedures for the patients with valvular heart disease (VHD) which resulted in significant improvement in survival and patients’ quality of lives\(^1\). In the last 5 decades the etiology of VHD has changed in the developed countries. A significant decrease in the occurrence of rheumatic fever and its sequelae thanks to the preventive vaccination, medications, expansion in expertise of detecting the heart pathologies with better understanding of the new VHD causes are the main basis of this change.

VHD can affect single or multiple valves with different pathologies. Boudoulas et al (1994) reported the VHD etiologies in 7 categories: 1) Heritable-congenital causes of valvular heart disease e.g., floppy mitral valve with mitral valve prolapse, bicuspid aortic valve, and the Marfan syndrome; 2) Inflammatory-immunologic causes such as rheumatic fever, acquired immune deficiency syndrome, endocardial proliferative disorders, and antiphospholipid syndrome; 3) Myocardial dysfunction-ischemic cardiomyopathy, dilated or hypertrophic cardiomyopathy-resulting in valvular heart disease; 4) Diseases and disorders of other organs as causes of valvular heart disease, e.g., chronic renal failure and carcinoid heart disease; 5) Valvular heart disease related to aging: calcific aortic stenosis and mitral annular calcification; 6) Valvular disease following interventions such as valvuloplasty, valve reconstructive surgery, valve replacement and drugs and physical agents, radiation therapy and trauma. The Medical Ethics Committee of Tabriz University of Medical Science approved the research project.

Recognition of the current status of the etiologies of VHD in a country may result in implementation of effective preventive measures that could help health programming. This multi-center project was designed to address this question. This is an analysis of valvular cardiac surgery patients of 6 major cardiac surgery centers in Iran as a comprehensive report of etiologies of VHD in Iran.

Methods

This prospective study included 3418 patients. Participants were consecutive patients registered under VHD in the cardiology departments of the authors' institution over the past 5 years in 6 major hospitals of cardiac surgeries in Iran [Tehran (capital city of Iran), Tabriz (located in North west of Iran), Mashhad (located in North East of Iran), shiraz (located in Center of Iran), Kermanshah (located in North west of Iran), Ahvaz (located in South west of Iran)] who were candidates of valvular heart surgery. We included 5 categories of VHD etiologies including Rheumatic, Ischemic, Infectious, Congenital and Degenerative.

Degenerative VHD is related to aging (calcific aortic stenosis and mitral annular calcification), following interventions such as valvuloplasty, valve reconstructive surgery, valve replacement and drugs and physical agents, radiation therapy and trauma. The Medical Ethics Committee of Tabriz University of Medical Science approved the research project. Etiologic and pathologic data of the VHDs of the operated patients were based on pathologic reports (for replaced valves) or gross detections of the surgeons (for repaired valves). Date regarding age and sex were also retrieved. Other medical conditions including rheumatic fever, drug abuse, addiction, congenital heart disease, previous interventional valvuloplasty, previous valve repair surgery, using specific medications, cancer and trauma were also recorded. Some of the patients had involvement of more than one valve. Data were analyzed, using SPSS (11) [SPSS Inc, Chicago, 11, USA] software. A descriptive analysis [mean, standard deviation (SD)] was conducted for each variable.

Results

The mean age of subjects was 43.98±14.45 years (aged between 2 to 86 year old). Amongst the whole subjects group, 1616 (47.27\%) were male and 1802 (52.73\%) were female. Approximately 46\% (1572) of all patients had Mitral valve surgery. The percentage of Aorta, Tricuspid, Pulmonary, Mitral & Aorta, Mitral & Tricuspid, Mitral & Aorta & Tricuspid Surgeries were 1161 (33.98\%), 28 (82\%),
25(0.74%), 576(16.84%), 34(0.99%), 22 (0.66%) respectively (Table 2). Among subjects who had Mitral valve surgery the male/ female ratio was: 638/934 and the mean age was 46.19±14.26; 842 (24.62%) had rheumatic valve disease, 327(9.56%) had Ischemic valve disease, 68 (1.99%) had infectious valve disease, 71(2.08%) had congenital valve disease and 264(7.72%) had degenerative valve disease (Table 1). Amongst the patients with Mitral valve surgery the male/ female ratio was: 638/934 and the mean age was 46.19±14.26; 842 (24.62%) had rheumatic valve disease, 327(9.56%) had Ischemic valve disease, 68 (1.99%) had infectious valve disease, 71(2.08%) had congenital valve disease and 264(7.72%) had degenerative valve disease (Table 1). Among patients who had Aorta valve surgery the male/ female ratio was: 656/505 and the mean age were 49.38±18.43; 549 (16.07%) had rheumatic valve surgery; 273 (7.99%) had ischemic valve disease, 45 (1.32%) had infectious valve disease, 88(2.58%) had congenital valve disease and 206(6.03%) had degenerative valve disease (Table 1). Amongst the patients with Aorta valve surgery the male/ female ratio was: 656/505 and the mean age were 49.38±18.43; 549 (16.07%) had rheumatic valve surgery; 273 (7.99%) had ischemic valve disease, 45 (1.32%) had infectious valve disease, 88(2.58%) had congenital valve disease and 206(6.03%) had degenerative valve disease (Table 1). Among patients who underwent Tricuspid surgery, the male/ female ratio was: 20/8 and the mean age was 33.80±14.48; 16 (0.35%) had rheumatic valve disease, 8 (0.17%) had ischemic valve disease, 6 (0.13%) had infectious valve disease, 3(0.06%) had congenital valve disease and 5 (0.11%) had degenerative valve disease (Table 1).

Among patients who underwent surgery of two valves of mitral and aorta, the male/ female ratio was: 271/305 and mean age was 45.52±11.94; 296 (8.65%) had rheumatic valve disease, 133(3.98%) ischemic valve disease, 28 (0.82%) infectious valve disease, 23 (0.67%) congenital valve disease and 96 (2.81%) degenerative valve disease (Table 1). Among patients who underwent Tricuspid surgery, the male/ female ratio was: 20/8 and the mean age was 33.80±14.48; 16 (0.35%) had rheumatic valve disease, 8 (0.17%) had ischemic valve disease, 6 (0.13%) had infectious valve disease, 3(0.06%) had congenital valve disease and 5 (0.11%) had degenerative valve disease (Table 1).

Of the individuals who had pulmonary valve surgery the male/ female ratio was: 13/ 12 and mean age was 49.12±19.44; 12(0.36%) had rheumatic valve disease, 4(0.12%) had ischemic valve disease, 1(0.03%) had infectious valve disease, 1(0.03%) had congenital valve disease and 3(0.11%) had degenerative valve disease (Table 1).

Amongst the patients with Mitral & Tricuspid valve surgery had Mitral valve surgery the male/ female ratio was: 10/24 and mean age was 45.52±11.94; 296 (8.65%) had rheumatic valve disease, 133(3.98%) ischemic valve disease, 28 (0.82%) infectious valve disease, 23 (0.67%) congenital valve disease and 96 (2.81%) degenerative valve disease (Table 1).

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Age Distribution of the patients with different valvular disease Of the all patients 38(1.11%) were under 10 year old, 124 (3.62%) were between 10-19 year old, 292 (8.54%) were between 20-29 year old, 561(16.41%) were between 30-39 year old, 910(26.62%) were between 40-49 year old, 742(21.18%) were between 50-59 year old, 556(16.26%) were between 60-69 year old and 213(6.23%) were 70 year old and over. The most patients with rheumatic valve disease were between 40-49 year old. Majority of patients with ischemic, infectious, congenital and degenerative diseases were between 40-49 year old, 30-39 year old, 20-29 year old and 40-49 year old respectively (Table 2). Data regarding age distribution of patients who underwent valvular surgery is shown in Table 2.
Table 1- Pathology distribution and age characteristics of the patients with different valvular heart surgery.

<table>
<thead>
<tr>
<th>Valves</th>
<th>Number (n)</th>
<th>M</th>
<th>F</th>
<th>Total</th>
<th>Age (mean±SD)</th>
<th>M</th>
<th>F</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mitral (45.97%)</td>
<td>1572</td>
<td>511</td>
<td>191</td>
<td>702</td>
<td>46.19±14.26</td>
<td>43.84±11.87</td>
<td>45.84±11.26</td>
<td>45.84±11.72</td>
</tr>
<tr>
<td>Aorta (33.98%)</td>
<td>1161</td>
<td>250</td>
<td>123</td>
<td>373</td>
<td>49.3±11.39</td>
<td>49.2±11.37</td>
<td>49.2±11.37</td>
<td>49.2±11.37</td>
</tr>
<tr>
<td>Tricuspid (0.82%)</td>
<td>28</td>
<td>5</td>
<td>2</td>
<td>7</td>
<td>33.80±14.48</td>
<td>43.5±11.85</td>
<td>43.5±11.85</td>
<td>43.5±11.85</td>
</tr>
<tr>
<td>Pulmonary (0.74%)</td>
<td>576</td>
<td>164</td>
<td>69</td>
<td>233</td>
<td>49.12±19.44</td>
<td>44.53±20.48</td>
<td>44.53±20.48</td>
<td>44.53±20.48</td>
</tr>
<tr>
<td>Mitral&amp; Aorta (16.84%)</td>
<td>576</td>
<td>164</td>
<td>69</td>
<td>233</td>
<td>49.12±19.44</td>
<td>44.53±20.48</td>
<td>44.53±20.48</td>
<td>44.53±20.48</td>
</tr>
<tr>
<td>Mitral&amp; Tricuspid (0.66%)</td>
<td>22</td>
<td>19</td>
<td>9</td>
<td>28</td>
<td>38.36±10.66</td>
<td>43.52±9.87</td>
<td>43.52±9.87</td>
<td>43.52±9.87</td>
</tr>
</tbody>
</table>

Values expressed as Mean± SD; figures in italic font represent the percentage of the group from total sample population. The numbers in parentheses are standard deviations.
In the present study, rheumatic VHD was found to be the most common etiology of VHD in Iran. Rheumatic VHD constitutes a major health problem in developing countries. For instance, Padmavati (1980), reported that 32-50% of all cardiac cases result from rheumatic fever in India. However Thakur et al (1996) reported that almost 2 million children were affected by rheumatic fever in India. Although, based on the progression of vaccination, antibiotic therapy and primary and secondary preventions the rheumatic VHD has declined in Iran compared to previous reports, it still remains one of the most important health system challenges.

The most frequently involved valves in our study, consistent with the other reports were isolated mitral and isolated Aort valve disease.

Although the valve surgery on isolated tricuspid and isolated pulmonary valves were very uncommon, the majority of involvements of these valves were rheumatic. These findings clearly indicate that the main cause of almost all valve surgeries is due to rheumatic involvement.

Upon our findings, majority of the patients with rheumatic VHD were between 40-60 years old, which is not consistent with the findings of other developing countries. According to the report of Nazarian (1978) the pathological features of the rheumatic valves in Iran are quite different from what is seen in western populations. This researcher described that three types of gross pathological features could be seen in Iran and in the third type the cusps are moderately thickened with short chordae tendineae with various degrees of calcification. Such pattern is seen usually in the 4th decades of life and is more frequent in males. Our findings showed consistency with Nazarian report.

Interestingly we witnessed 6 patients with isolated native infective non-rheumatic tricuspid. There was another case report from Iran with two similar cases. As shown in Table 2 most patients with ischemic VHD are between 40-49 that is because of the high prevalence of ischemic heart disease in this age interval in Iran. We found that mitral was the most frequently involved valve with infective VHD. This is exactly consistent with the previous report of Ishikawa et al from Japan.

The percentage of the patients with degenerative VHD was about 17% of the valvular pathologies. It seems that this finding is not consistent with the report of Horstkotte in 2008 from central Europe; in which the vast majority of patients with valvar heart disease had degenerative aortic valve stenosis or mitral regurgitation.

It is estimated that the prevalence of aortic stenosis is 2% of the population >65 years of age (an additional 29% have aortic valve sclerosis, i.e., thickening and calcification and cuspal thinning of a trileaflet aortic valve in the absence of ventricular outflow obstruction) in the western societies.

There are a large number of patients with congenital VHD in the age interval between 20-29 and there is not enough screening for detecting congenital VHD in the lower age so many patients with congenital VHD remain undiagnosed until the third decade of life in Iran. It should also be highlighted that VHDs still comprise a main health problem which will increase with the aging population.

Table 2- Distribution of various valvular hear diseases in different age decades.

<table>
<thead>
<tr>
<th>Pathology</th>
<th>Age</th>
<th>Under 10</th>
<th>10-19</th>
<th>20-29</th>
<th>30-39</th>
<th>40-49</th>
<th>50-59</th>
<th>60-69</th>
<th>&gt;70</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rheumatic</td>
<td></td>
<td>11</td>
<td>25</td>
<td>66</td>
<td>222</td>
<td>474</td>
<td>459</td>
<td>325</td>
<td>109</td>
</tr>
<tr>
<td>Ischemic infection</td>
<td></td>
<td>7</td>
<td>3</td>
<td>79</td>
<td>164</td>
<td>251</td>
<td>135</td>
<td>110</td>
<td>44</td>
</tr>
<tr>
<td>congenital degenerative</td>
<td></td>
<td>0</td>
<td>0</td>
<td>26</td>
<td>66</td>
<td>33</td>
<td>11</td>
<td>11</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Total(%)</td>
<td>38(1.11)</td>
<td>124(3.62)</td>
<td>292(8.54)</td>
<td>561(16.41)</td>
<td>910(26.62)</td>
<td>724(21.18)</td>
<td>556(16.26)</td>
<td>213(6.23)</td>
</tr>
</tbody>
</table>

Discussion

In the present study, rheumatic VHD was found to be the most common etiology of VHD in Iran. Rheumatic VHD constitutes a major health problem in developing countries. For instance, Padmavati (1980), reported that 32-50% of all cardiac cases result from rheumatic fever in India. However Thakur et al (1996) reported that almost 2 million children were affected by rheumatic fever in India. Although, based on the progression of vaccination, antibiotic therapy and primary and secondary preventions the rheumatic VHD has declined in Iran compared to previous reports, it still remains one of the most important health system challenges.

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There are a large number of patients with congenital VHD in the age interval between 20-29 and there is not enough screening for detecting congenital VHD in the lower age so many patients with congenital VHD remain undiagnosed until the third decade of life in Iran. It should also be highlighted that VHDs still comprise a main health problem which will increase with the aging population.

Study limitations:

This study has several limitations that deserve to be mentioned. First of all this is a descriptive study. Also, collecting the other related data including type of surgeries (repair or replacement) and conducting the other surgeries along with valvular surgery (such as coronary artery bypass graft) could have

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improved the results. Second, we did not analyze the different subtypes of any pathologies thus it is not clear whether there was any relationship between the third type of rheumatic VHD and higher age in this study, as previously reported.\textsuperscript{12} It would be of interest to study the the degree of insufficiency and stenosis of the valves.

**Conclusion**

On the basis of available data from different areas in Iran it appears that rheumatic VHD is the most frequent type of pathology among patients undergoing valvular surgery. The relatively high age of the patients with rheumatic VHD emphasizes the priority of this health problem in Iran which requires particular attention, especially in terms of prevention and also treatment. Preventive measures for rheumatic VHD should focus on primary prevention to turn away the first attack of carditis and intensification of secondary prophylaxis through improved education and motivation of patients and physicians. Further investigations are required to assess different types of rheumatic VHD in different ages.

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