Abstract. – Background: Some of theories try to explain the insurgence of atrial fibrillation (AF) in patients with acute articular rheumatism (AAR). These theories remind the close relation between AF and left atrium, or with valvular vitium degree, or monophasic action potential and histological cardiac structure. In 15 years of work in the academic Department of Heart and Big Vessels in Rome, the Authors studied 243 patients with mitral valvular disease post AAR before and after surgical manoeuvres.

Materials and Methods: Patients were divided in order to monitor atrium and ventricle morphological and functional modifications of the valve according to cardiac rhythm. Patients classification was based on surgical therapy adopted, kind of mitral disease and cardiac rhythm. An histological examination was performed, only in patients treated with valvular replacement. During the operation an histological examination in an atrial tissue fragment was performed. 243 patients with mitral valvular disease post AAR with indication in valvular adjustment were studied. The whole population was treated with mitral transcutaneous valvuloplasty (Group B – 130 patients) or with mitral valve replacement surgery (Group A – 113 patients). These two groups were divided: in Gr.A in Gr.A1 and Gr.A2, and Gr.B in Gr.B1 and Gr.B2, according to cardiac rhythm (sinus rhythm iSR, AF). These subgroups were also divided in Gr.A1SR, Gr.A1AF; Gr.A2SR, Gr.A2AF; Gr.A3SR, Gr.A3AF, according to mitralic disease’s kind (stenosis, stenosis/regurgitation, regurgitation). A complex screening were exerted to all patients using echocardio-doppler technology. Morphological parameters of atrium and ventricle, and functional parameters of mitral valve, aorta and tricuspid were evaluated. In Gr.A group patients during the operation were execute a biopic sampling from left atrium and a consecutive histological valuation.

Results: In Gr.A, mitral valve area (MtVA) arises smaller (p<0.01) in the group with AF, than those in SR. On the contrary, in subgroups of population of Gr.B there isn’t statistic dis-agreement (p>0.05). Left atrium volume arises elder in patients in AF than in patients in SR (p<0.01), either in patients of subgroups Gr.A1, Gr.A2 or in patients of the whole Gr.B before and after valvuloplasty. In the whole population Gr.B, either Gr.B1 or Gr.B2, left and right atrial volumes decrease eloquently (p<0.01) after valvuloplasty.

There’s no linear relationship (Pearson r<0.5) between the different subgroups of Gr.A (Gr.A1, Gr.A2, Gr.A3) and those of Gr.B according to mitral valve area (MtVA), volume and left atrial area. Left atrial biopsy shows in patients of SR a normal atrial tissue in the 48% of cases and lightly altered in remaining 52%. On the contrary in patients of AF there are strong anomalies in the 100% of cases.

Conclusions: According to histological view, atrial volumes variations and valvular area variations before and after surgical treatment, and according also to their comparisons in different groups, authors could assume that insurgence of AF and its chronicization could be an expression of a strong atrial myocardial histological alteration. Furthermore while starting moment of AF genesis is characterized by histological alterations of atrial myocardium (expression of rheumatic chronic disease), its chronicization hands to anatomic-volumetric progressive deterioation of the atrial dysfunction.

Key Words: Mitral valve, Atrial fibrillation, Acute articular rheumatism, Sinus rhythm, Left atrium.

Introduction

In the latest 30 years of the last century, rheumatic disease’s incidence in the world fortunately decreased, because of many factors like
scientific evolution and social-sanitary improvement. In the second half of XX century, the incidence was one case in one thousand people every year. Between 2000 and today in some geographic areas of east Europe, in Australia and Africa a recurrence of the rheumatic disease was noted. So it becomes object of careful observation in several schools1-8.

In the past the common association between mitral valve disease and atrial fibrillation was an argued item. The disease’s extinction didn’t answer to the most important question: if and which physiopathological mechanisms linked these two diseases.

The physiopathological link between the disease could be9:

- the anatomic and functional alterations and electrophysiological modifications observable in rheumatic disease’s history,
- the lazy and progressive blood’s stagnation in the atrial chamber and its remoulding,
- the progressive thickening, fibrosis and calcification of the valvular system, could be the physiopathological link between the diseases.

From this point of view, it is not already clear if left atrium dilatation, left atrium wall alteration and mural thrombosis formation, that are observable in rheumatic valvular disease’s history, are the evolution of a slow subacute process of the incipient rheumatic disease or if they are associated to hemodynamic/electrophysiological modifications8,19.

The aim of this work was to research possible temporal and functional correlations between cardiac electrical activity (sinus rhythm or atrial fibrillation), atrium sizes, endangerment’s degree of the mitral valve system and histological conditions of the atrium wall.

### Materials and Methods

In Heart and Big Vessels Department of “La Sapienza” University of Rome, Italy, a population of 243 patients hospitalized and “in-office” followed was examined in 15 years. The patients mean value age were 50.4±10.3 years (range 14-78 years), 63 males (M) were 51.5±10.4 years, and 180 females (F), were 50.8±9.3 years. Inclusion’s criterions in the study were:

1. Rheumatic disease not in active stage.
2. Isolated mitral valve disease even if “tricuspidalized” (allowed aortic insufficiency of light degree)17.
3. Indication to valvular adjustment in dependence on mitralic valve surface indexed and on NYHA functional class.
4. Lack of other pathologies like thyroid disease, acute renal insufficiency or hard chronic, liver failure, arterial hypertension, ictus or former TIA episode.
5. Checks in patients submitted to mitral transcutaneous valvuloplasty.
6. Checks in patients submitted to mitral valve substitution (mechanic or biological).

All patients had normal arterial pressure values and had no altered hematochemical values about proteins, glucose and lipids.

All subjects, afterward enough information and after received their accordance, were submitted to periodic sanitary checks (6-8 months). On average each patient was submitted to 2 checks before the correction and to 12±2 checks the surgical treatment.

During the check a medical examination was accomplished. Hematochemical tests, colour Doppler echocardiography and, if required, transesophageal TEE, external electrocardiogram, unbloody measurement of humeral arterial pressure were performed.

130 of the 243 patients were submitted on mitralic percutaneous valvuloplasty (using Inoue’s catheter)18,19. The other 113 patients were submitted to a valve substition’s surgery with valvular prosthesis (mechanical kind in 93 cases and biological in 20).

Indication to valvular adjustment in dependence to mitral percutaneous valvuloplasty20-21 was choose according to clinic conditions and TTE-TEE test22, if there was:

1. Mitral regurgitation (higher and light-medium degree);
2. Valve anomaly and malformation and under-valvular system (Wilkins and Ried “score”)23;
3. Presence of thrombosis in left atrium.

For statistical reasons 243 patients were mostly divided in two groups: Group A (113 patients) submitted to mitral valve substitution surgery (Mt.V.S), and Group B (130 patients) submitted to mitral percutaneous valvuloplasty (Mt.P.V). According to pre-surgery prevalent valve disease
Gr.A group was divided in the following three subgroups (Gr.A1, Gr.A2, Gr.A3):

Gr.A1 → patients with isolated mitral stenosis;
Gr.A2 → patients with mitral stenosis/regurgitation;
Gr.A3 → patients with pure mitral regurgitation.

Afterward according to sinus rhythm (SR) or atrial fibrillation (AF) each subgroups patients, according to sinus rhythm (SR) or atrial fibrillation (AF) were divided in further two subgroups: Gr.A1SR, Gr.A1AF; Gr.A2SR, Gr.A2AF; Gr.A3SR, Gr.A3AF.

In Gr.B group were present only patients with isolated mitral stenosis. This group was divided in two groups Gr.B1 (before valvuloplasty) and Gr.B2 (after valvuloplasty). Each group was divided in four subgroups according to cardiac rhythm’s kind (Gr.B1SR, Gr.B1AF; Gr.B2SR, Gr.B2AF). Table I shows all described groups.

After surgical treatment population from Gr.A group wasn’t evaluated by statistical analysis. That was because athromboty due to the operation and auricle’s closure should invalidated findings.

**Lab Test**

General chemical tests for possible phlogosis and specific for immunity research to rheumatic disease and evaluation of hepatic-renal function and glucidic-lipidic complement.

**Echocardiography**

Transthoracic echocardiography (TTE) and transesophageal (TEE) tests were effectuated in each patient in quiet condition through echocardiograph ATL. Patients were invited to lie down on the litter and to put down in left lateral decubitus elevated in about 30°, TTE or TEE were executed using standard projections and finding measures, following American Society of Echocardiography standards.

**Statistical Analysis**

The average and respective standard deviation was evaluated in data statistic elaboration. In order to compare values average it was used Student t test with two samples in discordant vari-
ance and with two codas. A linear correlation between different groups and in the group itself was executed (Pearson) with homogeneous and paired parameters.

Results

The composition of groups and subgroups are summarized in Table II to VI.

The average age is significantly ($p<0.001$) higher in the patients suffering to atrial fibrillation (AF) in relation to those in sinus rhythm (SR), both in Gr.B ($57 \pm 8.4$ vs $42.3 \pm 11.4$) than in Gr.A1 ($55.8 \pm 8.4$ vs $41.5 \pm 11.5$) and Gr.A2 ($57.5 \pm 8.7$ vs $43.1 \pm 12.3$) (Table II).

In preoperatory phase of Gr.A:

- There is not statistical difference on functional class between the various groups ($p>0.05$).
- In the Gr.A1, Mitral Valve Area (MtVA) is smaller ($p<0.01$) in the patients with AF than in SR (Table III).
- The left atrium diameter is greater in patients with AF in relation to those in both the SR Gr.A1 and Gr.A2 (Table II).
- The area and left atrial volume are significantly ($p<0.001$) greater in patients with AF in relation to those in both the SR Gr.A1 and Gr.A2, while in Gr.A3 this difference is evident only for the area of the left atrium (Table II).
- Area and volume of the right atrium ($p<0.001$) are higher in the AF group in than SR in both the Gr.A1 and in Gr.A2 (Table II).

In the Group B it is observed that:

- The medium age of the Gr.BSR vs Gr.BAF is statistically inferior.
- Statistically significant difference ($p>0.05$) between the two subgroups (Gr.B1SR vs Gr.B1AF), before the valvuloplastic surgery does not exist.
- A difference ($p<0.001$) between Gr.BSR and Gr.BAF in the left atrial volume both before the valvuloplastic and after valvuloplastic surgery ($60.6 \pm 16.8$ cm$^3$ vs $96 \pm 42$ cm$^3$), is observed. This volume is greater in the patients with AF regarding those in SR.
- A significant ($p<0.01$) reduction of the left and right atrial volumes is observed after the valvuloplastic both in the Gr.BSR (Gr.B1SR $81.6 \pm 18.4$ cm$^3$ vs Gr.B2SR $60.6 \pm 16.8$ cm$^3$) and in Gr.BAF (Gr.B1AF $119 \pm 45.7$ cm$^3$ vs Gr.B2AF $96 \pm 42$ cm$^3$) (Table II).

Data regarding patients with mitral regurgitation (Gr.A3) show that in patients suffering from AF, right atrial volume and the severity of tricuspid regurgitation are significantly higher than in the patients with SR ($p<0.05$) There is also a statistically significant linear correlation between these two parameters ($r>0.7$) in patients both in the AF and SR groups.

There is no correlation between mitral regurgitation and left atrial volume in Gr.A3AF, while there is a correlation coefficient ($r=0.7$) in Gr.A3SR (the corresponding subgroup but in SR).

Functional Class NYHA has been reduced progressively from the preoperative value, always maintaining statistical significance; from $2.82 \pm 0.45$ to $0.9 \pm 0.4$ (post-surgery) ($p<0.001$), from $2.82 \pm 0.45$ to $0.5 \pm 0.3$ (after 6 months) ($p<0.001$). The cardiac rhythm has remained unchanged in all the cases with the exception of a patient who has returned to SR after valvuloplastic surgery, maintaining this rhythm until the last control.

In 37% of the patients of the Gr.A in the immediate post-operative period were in SR (electrical cardioversion at the end of the EC), but they gradually come back in AF within the 10 post-operative day in spite of the antiarrhythmic therapy.

For the detailed results it is possible to consult Tables II, III, IV and V.

From the results of biopsies performed on the left atrium in all patients of Gr.A during the intervention (Table VI) it has been observed that in
Table II. Results.

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</thead>
<tbody>
<tr>
<td>GrA1</td>
<td>41.5 ± 11.5</td>
<td>23 F 1 M</td>
<td>59.8 ± 12</td>
<td>46 ± 7.2</td>
<td>23 ± 5.8</td>
<td>18.7 ± 6.1</td>
<td>74 ± 33</td>
<td>14 ± 3</td>
</tr>
<tr>
<td></td>
<td>55.8 ± 8.4</td>
<td>17 F 3 M</td>
<td>55 ± 6.2</td>
<td>52.8 ± 8.8</td>
<td>33.4 ± 8.3</td>
<td>22.3 ± 6.2</td>
<td>110.5 ± 36</td>
<td>23 ± 6</td>
</tr>
<tr>
<td>GrA1AF</td>
<td>55.8 ± 8.4</td>
<td>1 M</td>
<td>64.5 ± 9</td>
<td>45.7 ± 8.4</td>
<td>23 ± 7</td>
<td>19.1 ± 5.8</td>
<td>71 ± 32.2</td>
<td>49.7 ± 22</td>
</tr>
<tr>
<td></td>
<td>57.3 ± 13.4</td>
<td>3 M</td>
<td>59 ± 10</td>
<td>38.7 ± 16.6</td>
<td>147.4 ± 87.3</td>
<td>12.8 ± 3.3</td>
<td>14.2 ± 2.6</td>
<td>21.3 ± 8.5</td>
</tr>
<tr>
<td>GrA2</td>
<td>62.8 ± 10.4</td>
<td>3 F 3 M</td>
<td>66.6 ± 14.8</td>
<td>46.6 ± 6.5</td>
<td>23.6 ± 4.1</td>
<td>16.4 ± 3.6</td>
<td>117.6 ± 59.6</td>
<td>14 ± 3</td>
</tr>
<tr>
<td></td>
<td>59 ± 11.3</td>
<td>6 F 3 M</td>
<td>63.4 ± 10.2</td>
<td>54.5 ± 7.6</td>
<td>29.8 ± 10</td>
<td>57.7 ± 52.8</td>
<td>118.2 ± 47.2</td>
<td>21.2 ± 4.2</td>
</tr>
<tr>
<td>GrA3</td>
<td>42.3 ± 11.4</td>
<td>56 F 31 M</td>
<td>58.3 ± 12</td>
<td>43.9 ± 7.4</td>
<td>16.1 ± 8</td>
<td>81.6 ± 18.4</td>
<td>58.6 ± 15.1</td>
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</tr>
<tr>
<td></td>
<td>57 ± 8.4</td>
<td>25 F 18 M</td>
<td>56.4 ± 6</td>
<td>58.3 ± 7.4</td>
<td>22.7 ± 10.5</td>
<td>119 ± 45.7</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>GrB1</td>
<td>42.5 ± 11.4</td>
<td>57 F 31 M</td>
<td>65.6 ± 15</td>
<td>39.4 ± 8.2</td>
<td>14.2 ± 6</td>
<td>60.6 ± 16.8</td>
<td>43.5 ± 13.3</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>57 ± 8.6</td>
<td>24 F 18 M</td>
<td>57.5 ± 4.5</td>
<td>51.7 ± 13</td>
<td>17.8 ± 4.3</td>
<td>96 ± 42</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>GrB2</td>
<td>42.5 ± 11.4</td>
<td>57 F 31 M</td>
<td>65.6 ± 15</td>
<td>39.4 ± 8.2</td>
<td>14.2 ± 6</td>
<td>60.6 ± 16.8</td>
<td>43.5 ± 13.3</td>
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</tbody>
</table>

SR = sinus rhythm; AF = atrial fibrillation; EF = ejection fraction; L. atrium. d.= left atrium diameter; L. atrium area = left atrium area; L. atrium vol. = left atrium volume; R. atrium area = right atrium area; R. atrium vol. = right atrium volume; Syst. = atrial systole; Diast. = atrial diastole.
**Table III. Results.**

<table>
<thead>
<tr>
<th>Groups</th>
<th>Lv. e-d. d</th>
<th>Lv. e-s. d</th>
<th>S.F.</th>
<th>MtVA$^{2D}$</th>
<th>MtVA$^{CW}$</th>
<th>MtR</th>
<th>AoR</th>
<th>TrR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gr.A1</td>
<td>46.7 ± 4.1</td>
<td>30.5 ± 6.1</td>
<td>33.5 ± 8.6</td>
<td>1.45 ± 0.47</td>
<td>1.36 ± 0.49</td>
<td>0.75 ± 0.29</td>
<td>0.96 ± 0.26</td>
<td>1.97 ± 0.76</td>
</tr>
<tr>
<td>Gr.A1SR</td>
<td>45.5 ± 4.2</td>
<td>32.5 ± 5.2</td>
<td>29.8 ± 8</td>
<td>1.1 ± 0.26</td>
<td>1.03 ± 0.25</td>
<td>0.71 ± 0.27</td>
<td>1.41 ± 0.3</td>
<td>2.24 ± 0.86</td>
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<tr>
<td>Gr.A2</td>
<td>50.2 ± 6.7</td>
<td>32.8 ± 6.4</td>
<td>35.4 ± 6.8</td>
<td>1.6 ± 0.39</td>
<td>1.57 ± 0.46</td>
<td>1.47 ± 0.47</td>
<td>1.29 ± 0.57</td>
<td>1.88 ± 0.64</td>
</tr>
<tr>
<td>Gr.A2SR</td>
<td>49.4 ± 7.4</td>
<td>33.6 ± 6.7</td>
<td>31.2 ± 8.8</td>
<td>1.5 ± 0.4</td>
<td>1.38 ± 0.4</td>
<td>1.89 ± 0.82</td>
<td>1.1 ± 0.4</td>
<td>2.37 ± 0.72</td>
</tr>
<tr>
<td>Gr.A3</td>
<td>59 ± 10.3</td>
<td>30.7 ± 4.5</td>
<td>38.6 ± 12</td>
<td>3.74 ± 0.58</td>
<td>3.66 ± 0.76</td>
<td>2.6 ± 0.55</td>
<td>1 ± 0</td>
<td>1.1 ± 0.22</td>
</tr>
<tr>
<td>Gr.A3SR</td>
<td>57.7 ± 5.8</td>
<td>36.8 ± 4.6</td>
<td>33.8 ± 6.5</td>
<td>3.5 ± 0.9</td>
<td>3.6 ± 0.7</td>
<td>3.25 ± 0.76</td>
<td>1 ± 0.71</td>
<td>1.67 ± 0.61</td>
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<td>Gr.B1</td>
<td>47.5 ± 5</td>
<td>31.2 ± 7</td>
<td>33.4 ± 7.8</td>
<td>0.95 ± 0.05</td>
<td>1.09 ± 0.23</td>
<td>0.5 ± 0.2</td>
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<td>Gr.B1SR</td>
<td>48.8 ± 3.9</td>
<td>35.2 ± 6</td>
<td>28.7 ± 4</td>
<td>1.1 ± 0.2</td>
<td>1.05 ± 0.16</td>
<td>0.5 ± 0.15</td>
<td>1 ± 0.3</td>
<td>1.45 ± 0.6</td>
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<td>Gr.B2</td>
<td>48.3 ± 4</td>
<td>29.8 ± 6</td>
<td>36.7 ± 9.2</td>
<td>2.37 ± 0.37</td>
<td>2.28 ± 0.47</td>
<td>0.98 ± 0.62</td>
<td>0.85 ± 0.4</td>
<td>0.5 ± 0.4</td>
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<tr>
<td>Gr.B2SR</td>
<td>50.3 ± 5</td>
<td>34.8 ± 7</td>
<td>29.5 ± 3.8</td>
<td>2.06 ± 0.25</td>
<td>2.14 ± 0.44</td>
<td>0.93 ± 0.48</td>
<td>1.05 ± 0.2</td>
<td>1.2 ± 0.5</td>
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</tbody>
</table>

Lv. e-d. d = left ventricular end-diastolic diameter; Lv. e-s. d = left ventricular end systolic diameter; S.F. = shortening fraction; MtVA$^{2D}$ = mitral valve area 2D; MtVA$^{CW}$ = mitral valve area CW; MtR = mitral regurgitation; AoR = aortic regurgitation; TrR = tricuspid regurgitation.

Hemodynamic grade of regurgitation: (±) = 0.5; (+) = 1; (++) = 2; (+++) = 3; (++++) = 4.
<table>
<thead>
<tr>
<th>Groups</th>
<th>AGE</th>
<th>FC NYHA</th>
<th>MtVA</th>
<th>LA.D</th>
<th>LAA</th>
<th>LAV</th>
<th>AV.Grad</th>
<th>RAV</th>
<th>TrR</th>
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</thead>
<tbody>
<tr>
<td>Gr.A₁SR ↔ Gr.A₁AF</td>
<td>p&lt;0.001</td>
<td>NS</td>
<td>p&lt;0.01</td>
<td>p&lt;0.01</td>
<td>p&lt;0.001</td>
<td>p&lt;0.001</td>
<td>–</td>
<td>p&lt;0.001</td>
<td>NS</td>
</tr>
<tr>
<td>Gr.A₂SR ↔ Gr.A₂AF</td>
<td>p&lt;0.001</td>
<td>NS</td>
<td>NS</td>
<td>p&lt;0.01</td>
<td>p&lt;0.001</td>
<td>p&lt;0.001</td>
<td>–</td>
<td>p&lt;0.001</td>
<td>p&lt;0.05</td>
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<tr>
<td>Gr.A₃SR ↔ Gr.A₃AF</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>p&lt;0.01</td>
<td>NS</td>
<td>–</td>
<td>p&lt;0.05</td>
<td>p&lt;0.05</td>
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<tr>
<td>Gr.B₁SR ↔ Gr.B₁AF</td>
<td>p&lt;0.001</td>
<td>NS</td>
<td>NS</td>
<td>p&lt;0.01</td>
<td>NS</td>
<td>p&lt;0.001</td>
<td>p&lt;0.05</td>
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<td>–</td>
</tr>
<tr>
<td>Gr.B₂SR ↔ Gr.B₂AF</td>
<td>p&lt;0.001</td>
<td>NS</td>
<td>NS</td>
<td>p&lt;0.05</td>
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<tr>
<td>Gr.B₃SR ↔ Gr.B₃AF</td>
<td>–</td>
<td>p&lt;0.001</td>
<td>p&lt;0.001</td>
<td>NS</td>
<td>NS</td>
<td>p&lt;0.01</td>
<td>p&lt;0.001</td>
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</tr>
<tr>
<td>Gr.B₄SR ↔ Gr.B₄AF</td>
<td>–</td>
<td>p&lt;0.001</td>
<td>p&lt;0.001</td>
<td>NS</td>
<td>NS</td>
<td>p&lt;0.01</td>
<td>p&lt;0.001</td>
<td>–</td>
<td>–</td>
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<tr>
<td>Gr.A₅SR ↔ Gr.A₅AF</td>
<td>–</td>
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FC NYHA = functional class NYHA; MtVA = mitral valve area; LA.D = left atrium diameter; LAA = left atrium area; LAV = left atrium volume; AV. Grad = atrium-ventricular gradient; RAV = right atrium volume; TrR = tricuspid regurgitation, NS = not significant.
the patients with SR the atrial tissue is normal in 44% of cases. The remaining 56% show a moderate increase in the parietal thickness in the 40% of cases and a reduction of parietal thickness in 6% of cases and normal thickness in 10% of cases. It has been observed moderate myocytes hypertrophy in 54% of cases, of which 44% is associated with increased parietal thickness and 10% with normal parietal thickness, a vacuolar slight degeneration in 6% of cases, mild interstitial fibrosis in 2% of cases, mild endocardial fibrosis in 4% of cases.

There are anomalies in 100% of patients in AF, including: moderate vacuolar degeneration in 77% of cases, a strong interstitial fibrosis in 75%, moderate presence of stretched fibres (70%), a strong adiposous replacement in 63% of cases, a moderate myocytes hypertrophy (54%), moderate pigmentary degeneration (48%), a normal endocardium (46%), moderate endocardial fibrosis (28%), a moderate increase in the parietal thickness (25%), a moderate colliquative myocytolysis (24%) of cases, presence of few but hypertrophic cellular elements (24%).

**Discussion**

To explain the history of the insurgence of atrial fibrillation in rheumatic valvulopathy, unanimously considered a pejorative device for the disease, many observations were made. These consideration are about morpho-functional

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**Table V.**

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</tr>
</thead>
<tbody>
<tr>
<td>MtV ↔ LAV</td>
<td>r&lt;0.5</td>
<td>r&lt;0.5</td>
<td>r&lt;0.5</td>
<td>r&lt;0.5</td>
<td>r&lt;0.5</td>
<td>r&lt;0.5</td>
<td>r&lt;0.5</td>
<td>r&lt;0.5</td>
</tr>
<tr>
<td>MR ↔ LAV</td>
<td></td>
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<tr>
<td>LAV before ↔ MtV after</td>
<td></td>
<td></td>
<td>r&lt;0.5</td>
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<tr>
<td>LAV after ↔ MtV before</td>
<td></td>
<td>r&lt;0.5</td>
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<tr>
<td>MtV + MR ↔ LAA</td>
<td>r&lt;0.5</td>
<td>r&lt;0.5</td>
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<tr>
<td>MtV + MR ↔ LAV</td>
<td>r&lt;0.5</td>
<td>r&lt;0.5</td>
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<tr>
<td>RAV ↔ TrR</td>
<td></td>
<td></td>
<td>r&lt;0.5</td>
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</tr>
</tbody>
</table>

MtVA = mitral valve area; LAV = left atrial volume; MR = mitral regurgitation; RAV = right atrial volume; TrR = tricuspid regurgitation; before = before-valvuloplastic; after = after-valvuloplastic.

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**Table VI.** Hystological atrial biopsy: results.

<table>
<thead>
<tr>
<th>Normal</th>
<th>Gr.AAF (63 pt)</th>
<th>Gr.AAF (50 pt)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal endocardium</td>
<td>0% (0)</td>
<td>44% (22 pt)</td>
</tr>
<tr>
<td>Reduction wall thickness</td>
<td>46% (29 pt)</td>
<td>6% (3 pt)</td>
</tr>
<tr>
<td>Increase wall thickness</td>
<td>25% (16 pt)</td>
<td>44% (22 pt)</td>
</tr>
<tr>
<td>Rare hypertrophic cells</td>
<td>24% (15 pt)</td>
<td></td>
</tr>
<tr>
<td>Myocyte hypertrophy</td>
<td>54% (34 pt)</td>
<td>54% (27 pt)</td>
</tr>
<tr>
<td>Vacuolar degeneration</td>
<td>77% (49 pt)</td>
<td>6% (3 pt)</td>
</tr>
<tr>
<td>Pigmentary degeneration</td>
<td>48% (30 pt)</td>
<td></td>
</tr>
<tr>
<td>Endocardial fibrosis</td>
<td>28% (18 pt)</td>
<td>4% (2 pt)</td>
</tr>
<tr>
<td>Interstitial fibrosis</td>
<td>75% (47 pt)</td>
<td>2% (1 pt)</td>
</tr>
<tr>
<td>Stretched fibers</td>
<td>70% (44 pt)</td>
<td></td>
</tr>
<tr>
<td>Adipose substitution</td>
<td>63% (40 pt)</td>
<td></td>
</tr>
<tr>
<td>Colliquative myocytolysis</td>
<td>24% (15 pt)</td>
<td></td>
</tr>
</tbody>
</table>

MtVA = mitral valve area; LAV = left atrial volume; MR = mitral regurgitation; RAV = right atrial volume; TrR = tricuspid regurgitation; before = before-valvuloplastic; after = after-valvuloplastic.
parameters (like left atrial increase and mitral valve area), or exclusively dependent from anatomopathological factors (like atrial myocardium histological ultrastructure) and from electrophysiological factors (like ionic flows through myocardiacites’ membrane canals).

Whereas rheumatic disease is the main etiologic factor of mitral valvulopathy, in this study it has been investigated the eventual role of histopathological substrate of rheumatic disease in atrial fibrillation’s genesis, starting from an accurate analysis of atrial and valvular morphology.

Synthesizing different research’s streaks in literature about atrial fibrillation’s genesis, it has been observed a slow evolution from the idea of the exclusive attention on left and right atrium dimensions (diameter over 45 mm or 65 mm) to a largest vision. This point of view alternates taking in exame either atrial wall histological structure or microelectrophysiological cells’ alteration, in particular a modification in myocardiacites’ monophasic action potential. Completing know how about atrial volume increase interfere hemodynamic factors, like mitral valvular area, left medium atrial pressures, pulmonary wedging pressures or Wedge and right medium atrial pressure, that determine an incessant stress in atrial wall.

In our study it was possible to observe:

- Left and right atrial dimensions, according to literatures, are significantly larger in AF patients than in SR patients.
- There’s no linear relationship between valvular alteration amount, stenosis (Gr.A1; Gr.B.), regurgitation (Gr.A2) or stenosis/regurgitation (Gr.A3), and left atrium increase.
- The seriousness of mitral stenosis is major in AF patients than in SR patients (group Gr.A1 and group with stenosis/regurgitation).
- In patients from Gr.B there’s no difference between AF and SR, in valvular area before and after valvuloplasty.

In patients from Gr.B there’s no statistically difference between AF and SR, in left atrial volume reduction before and after valvuloplasty.

Different behavior of the two groups in re-distribution of atrial volume according to valvular defect, could mean that straight nexus described in literature between AF and atrial volume, or between A and MtVA, or between AF and pathology degree is not so clear.

It’s important to remind that all patients in AF were submitted, following classic standards, to antiarrhythmic therapy to reinstate sinus rhythm. One patient in AF, submitted to percutaneous mitralic valvuoplasty, came back 5 days after sinus rhythm correction. All patients submitted to valvular substitution with prosthesis, egresses from operating room with a SR induced by cardioversion (37% in 113 patients), gradually returned in atrial fibrillation in 10 days after the surgery, despite antiarrhythmic therapy.

Atrial dimensions after surgery were not charged, because athrotomy and its mending determine an artificial modification in left atrial dimensions. This modification is not ponderable and could invalidate the measurement about the probable reduction induced. Instead, only by the MtVA modification or relate it with the atrial volumes of valvuoplasty group. The outcomes of histological analysis in 113 patients submitted to operation show in patients in AF more than a histological alteration in all microscope slides (100%). The most frequent was a vacuolar degeneration of the myocardiacite (77%), whereas in 75% of the cases there was an interstitial fibrosis; sprained fibers (70%) and ample adipose degeneration (63%) were less frequent.

In SR just the 56% of the microscope slides showed a modest alteration that consisted in cellular hypertrophy (54%). Fibrosis or vacuolar degeneration were slightly referred and present respectively in 2 and 6% of the group. From these data it can be deduced that atrial volume, significantly larger in patients in AF, can’t be considered strictly related to mitralic valve alteration’s entity, neither as the primary cause of arrhythmia. The cause of atrial fibrillation genesis have to be researched other where, instead atrial dimensions assume a function in a sequent step of physiopathological frame. It is possible to suppose that an essential role as primum movens in establishing of arrhythmia could be played by histological alterations found in this study of atrial myocardium of patients in AF, despite atrial biopsies belonging to patients in sinus rhythm bare of considerable and expressive alterations. The structural subversion found in presence of AF, and particularly cellular degeneration with a marked increase of interstitial fibrosis, can influence and impulse generation and propagation potential in atrial chamber.

And electrophysiological modifications able to
cause the arrhythmia can intervene. The presence of substitutive fibrosis, joined with a structural modification of myocardiocites, can explain the possible reduction of L canals of calcium and consequently the reduction of the calcium current (Ica) through the same canals. Ica’s reduction is been considered in several studies like the most important ionic modification present in myocardiocites of fibrillant atrium. To confirm this idea there are all those patients in chronic AF submitted to mitral valvoplasty: despite they improve their conditions with mitral valvular area’s increase, with right and left atrial volume’s reduction and with an enhancement in functional class (regressed from II-III to barely belonging to Ia), they rested in atrial fibrillation. Furthermore, it can be assumed, that histological alterations can cause the aberrations described and it can determine AF. Besides once AF is established it alters systolic-diastolic cardiac cycle, it produces a progressive modification in blood stagnation and in average atrial pressure, that determines a progressive aggravation of atrial volume. This thesis is supported by that there’s not a significant relationship between stenosis entity or mitral regurgitation and atrial dimensions. This evidences that hemodynamic factors are not the exclusive agents of atrial increasing. The only patient (Gr.B) in atrial fibrillation of recent insurgence (less than two weeks) before valvuloplasty, re-entered in sinus rhythm after five days. Before the dilatation with balloon, he was in anti-arrhythmic therapy (amiodarone in dosage 200 mg × 2 daily for 7 days, then 200 mg × 2 for 7 days and then 200 mg daily) and actually (after two years) still in SR and in treatment with amiodarone 200 mg daily for five days a week. The data related to left atrial volume, before and after valvuoplasty and valvular area before and after valvuloplasty, were in the average of the values related to belonging group. Respectively atrium was 80 cm³ vs 119±45.7 cm³ before valvuloplasty and 60 cm³ vs 96±42 cm³ after. Whereas MtVA was 1.1cm² before valvuloplasty 1.05±0.16 cm² and 1.9 vs 2.06±0.25 cm² after. Maybe the return of this patient (Gr.B) firstly fibrillant in SR after valvuloplasty is a consequence of two factors. First is that the AF was of recent insurgence (less than six months) and second is that the patient had a left atrial volume (before and after operation) clearly inferior compared to the average. So it can be assumed that in this patient all the actions described were still inexisten or in an early stage. Particularly that histological alteration is able to start AF and the vicious circle of structural subversion and atrial wall straining (that determines the persistent of arrhythmia) was not yet determined, so the antiarrhythmic action of the drug had worked. Finally it can be deduced that the initial moment in AF genesis can be recognized by histological alterations of atrial myocardium, that represent cardiac manifestation of rheumatic disease. This disease is rheumatic cardiopathy which concerns myocardium, endocardium and (in less proportion) pericardium.

Once it is established, AF concurs to progressive deterioration of atrial myocardium, already started for rheumatic cardiopathy, and so to progressive straining and increase of the atrium.

References

1) TIBAZARWA KB, VOLMINK JA, MAYOSI BM. The incidence of acute rheumatic fever in the world: A systematic review of population-based studies. Heart 2008; 94: 1534-1540.


Atrial fibrillation in rheumatic valvular disease


