CONCOMITANT ATRIAL FIBRILLATION IN PATIENTS WITH MITRAL VALVE DEFECTS

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A.G. Yambatrov, Physician, Cardiovascular Surgeon[1];
A.P. Medvedev, D.Med.Sc., Professor, Head of the Department of Hospital Surgery named after B.A. Korolyov[2]

[1]Republican Cardiological Dispensary, F. Gladrova St., 29A, Cheboksary, Chuvash Republic, Russian Federation, 428020;
[2]Nizhny Novgorod State Medical Academy, Minin and Pozharsky Square, 10/1, Nizhny Novgorod, Russian Federation, 603005

The current state of the problem of concomitant atrial fibrillation (AF) in patients with mitral valve defects was considered. The data on the epidemiology of mitral valve disease and the etiology and pathogenesis of atrial fibrillation were presented. The characteristics of the development of the heart rhythm disorder in patients with mitral valve disease and the possibilities of heart rhythm recovery after the valve surgery were showed. The probability of spontaneous recovery of sinus rhythm in these patients was found to be low especially in patients with persistent AF requiring concomitant interventions.

The history of the development of surgical techniques of atrial fibrillation management was reviewed. Now, a classic operation "Cox-Maze III" considered to be the "gold standard", has commonly been displaced by alternative technologies replacing a scalpel. The data on the modern devices for surgical ablation (cryoablation, microwave, ultrasound ablation) were presented. Currently, the most common method is the radiofrequency ablation (RFA) consisting in the use of AC current of 50 kHz to 1 MHz. There were reviewed the properties of the method, its varieties, advantages and limitations. Initially used monopolar ablation was shown to have relatively low efficiency and the higher probability of complications than bipolar ablation that came into use later. "Cox-Maze IV" operation using bipolar RFA demonstrates the efficiency comparable to the classical "Maze III". Despite certain advances in the surgical treatment of atrial fibrillation, the question of developing an optimal method able to be widely implemented with maximum efficiency and minimal complications was concluded to remain still open.

Key words: mitral valve; heart defect; atrial fibrillation; sinus rhythm; radiofrequency ablation.

According to the present knowledge, atrial fibrillation (AF) occurs in 1–2% of population [1–9]. Currently, over 6 million Europeans and 2.5 million Americans are subjects to this pathology, and according to prognoses, within the following 40–50 years its incidence will increase by 1.5–3 times [3, 6, 7, 10]. AF pathogenetic significance consists in the abolition of atrial transport function, cardiac rhythm irregularity, the increase of thromboembolism level that raises the risk of ischemic stroke by 2–5 times [3, 4]. AF associated stroke has higher mortality [9]. The factors associated with AF also include the increase of hospitalization frequency (over 30% of admissions for rhythm disturbance), progressive chronic heart failure, deterioration of patients' quality of life, and escalation of treatment costs. In the estimation of experts, annual costs of AF treatment is about 26 billion USD and from 372 million to 3.2 billion EURO in different European countries [3–5, 9, 11, 12]. About 30% of these expenses are directly related to AF presence [12].

Today there are two main "strategies" of AF management: rhythm control and heart rate (HR) control combined with the administration of oral anticoagulants. According to literature reports, in case of AF not associated with organic heart disease, the strategy selection does not affect life expectancy, just its quality, since a positive effect of sinus rhythm (SR) restoration is leveled by adverse effects of antiarrhythmics [3–5].

Along with an "isolated" form there is AF associated with structural pathology, e.g. valve defects are revealed in about 30 % (from 5.6 to 66.3 %) of AF patients [3, 4, 8]. In mitral valve (MV) diseases there is left atrial (LA) overdistension, and AF can be their first sign [3, 4]. In patients with mitral valve diseases and AF the complication risk and mortality increase by 1.5–2 times, and defect repair does not always

For contacts: Yambatrov Alexandr Georgievich, phone: 8(8352)62-83-99, +7 905-028-14-42; e-mail: yambatrov@gmail.com

result in SR restoration [13, 14]. SR significance can be explained by the fact that reconstructive operations on MV do not require further life-long oral anticoagulant therapy and become widespread [15].

The task health service sets today is not only to prolong life, but also improve its quality. The current situation made researchers and clinicians develop and introduce into clinical practice additional intraoperative measures aimed at SR restoration and maintenance in surgical correction of heart defects under artificial circulation.

Mitral valve diseases and atrial fibrillation

Currently, heart valve defects, and MV diseases in particular, is one of the most frequent cardiac pathologies. According to Euro Heart Survey, MV diseases among the patients admitted to cardiac or cardiac surgical departments, or followed up in outpatients departments have been found in 34.3 % of cases. In general population the frequency of mitral valve disease has been considerably increasing with age (from 0.5% in people under 45 to 9.5% in those over 75) [16]. Currently, mitral stenosis incidence in West Europe, in contrast to the Russian Federation, has decreased and amounts 27.7% of all mitral valve diseases due to the reduced rheumatic disease incidence [17–20]. The reports in literature show that in West European countries MV diseases are the diseases of middle-aged and elderly people, while in Russia, despite the advances of Russian medical science, they still remain the pathology of young people that makes the problem urgent in this country [16, 17].

Patients with mitral valve diseases are characterized by supraventricular arrhythmia, AF in particular (30–40%) [17, 21]. According to literature data, AF occurs in 17% of patients aged 21–30, 45% — aged 31–40, 60% — aged 41–50, and in 80% of those over 51 [22]. Among the patients with valve diseases (mainly, with MV pathology) requiring surgical management AF occurs in 30–84% of cases [23, 24]. AF in such patients is due to LA overdistension, therefore, timely removal of this pathogenetic factor can result in cardiac rhythm normalization. However, according to a number of studies, spontaneous SR restoration after mitral valve disease correction occurs only in a small number of patients (from 8.5 to 26 %) [14, 25, 26]. In literature there is contradictory information on the factors contributing to SR restoration and maintenance (which also includes patients after surgical management of AF) [24, 27, 28]. Most researchers distinguish such factors as AF duration and LA size [24, 29, 30].

Acute AF and, mainly, high HR reducing the period of diastolic filling and causing pressure increase in LA result in significant hemodynamic shifts in patients with MV diseases. AF occurs more frequently in elderly patients and has more negative prognosis: only 25% of patients have 10-year survival rate, in contrast to 46% for SR patients [17, 21]. AF presence in patients with MV diseases worsens the prognosis of postoperative survival, increases the risk of cardiac death, heart failure and stroke [17, 28, 31, 32]. Any AF form increases the risk of thromboembolic complications including acute cerebrovascular accident that reduces the advantages of valve-saving interventions on MV due to the necessity to use anticoagulant therapy [17, 25].

Atrial fibrillation etiology

AF etiology is not yet completely understood, currently there is known the list of diseases and conditions, which are the markers of general cardiovascular risk and/or cardiac damage, and not only etiological factors of AF [2–4]. AF is associated with a wide range of cardiovascular diseases and conditions: arterial hypertension, chronic heart failure, cardiomyopathies, atrial septal defect and other congenital heart diseases, chronic heart disease, etc [3]. In addition, recently, genetic factors and canalopathy are given the higher priority to [1, 2].

As stated before, LA overdistension in patients with MV diseases resulted from blood outflow disturbance and related structural alterations change electrophysiological characteristics of LA with the result that there occurs not only structural remodeling of atrial myocardium, but also the so called electrical remodeling [33]. AF in patients with mitral valve diseases occurs more frequently in elderly, and the duration and frequency of rheumatic fever in case of rheumatic etiology of the disease are of importance, since a rheumatic process in itself can result in fibrosis of different myocardial areas [17, 28, 34].

Pathogenesis and clinical aspects of atrial fibrillation

The main pathophysiological and clinical presentations of AF are irregular atrial activation, related mechanical atrial dysfunction and irregular ventricular contraction, hemodynamic changes and thromboembolic complications [4, 10].

The mechanism of AF formation has not been clear a great while, there have been varied opinions: numerous chaoitical cardiac impulses, focal electrical discharges, local reentry-activity with fibrillation conduction [2]. M. Haissaguerre and colleagues made a great contribution to the understanding of AF mechanisms, as they mapped the triggers of paroxysmal AF in entries of pulmonary veins in 94% of patients with LA having diameter under 5 cm, and extending from 1 to 4 cm inside the pulmonary vein [10, 35]. J. Cox created a model according to which AF starts near the pulmonary vein entry, where there is a transition zone between venous endothelium and LA endocardium [10, 36]. Due to the ganglia of autonomous nervous system located nearby, in this area it is possible to form macro-reentry circles, which result in premature contraction and by that form triggers. Cardiac impulse edge spreads through the LA from the pulmonary vein entry, becomes irregular going through the areas with different conduction velocity and refractory periods. Finally, one (or more) macro-reentry circle forms in one or both atria resulting in AF development (Fig. 1). Spontaneous or induced reentry circle termination results in SR restoration [10].

A key point in the understanding of persistent AF development is electrical remodeling. Organic heart diseases are known to cause progressive structural atrial

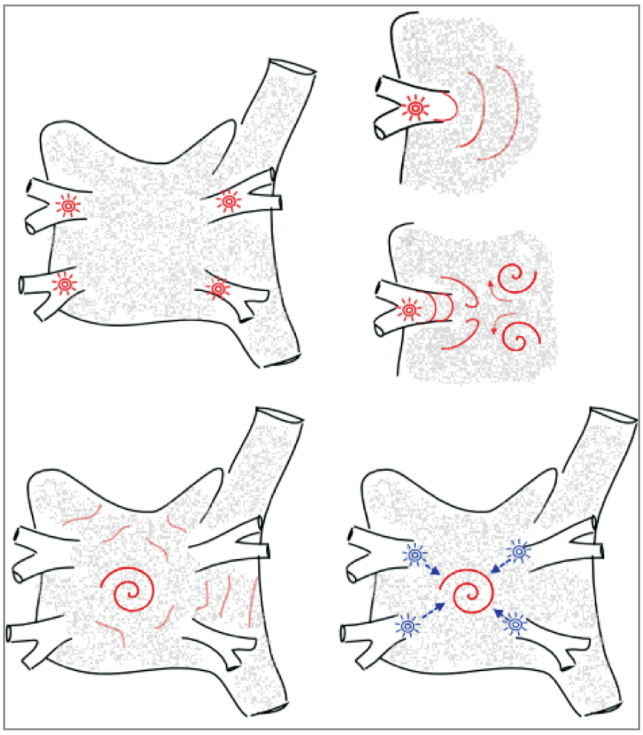

Fig. 1. The mechanism for the formation of reentry circles in the left atrium [2]

remodeling characterized by fibrosis growth resulting in electrical dissociation and conduction inhomogeneity and the formation of numerous reentry foci [3, 4, 33]. The following electrical remodeling consists in the changing of repolarization parameters of the cells involved in reentry circles resulting in the reduced duration of their action potential and refractory periods. These changes promote the maintenance of reentry circles. Otherwise, the longer the atrium fibrillates, the greater its susceptibility to fibrillation. While LA remodeling grows, the significance of triggers decreases that makes it difficult to manage a long-lasting persistent AF [10, 36].

Irregularity of cardiac contraction developing in AF patients has significant variety due to the fact that refractoriness of atrioventricular node acting as a filter is affected by autonomous nervous system. The frequency of ventricular contraction in such patients changes significantly throughout a day, mainly having a tendency to tachycardia [4].

As a consequence of irregularity, high frequency of ventricular contraction, the absence of coordinated atrial and ventricular contractions, hemodynamic changes develop. The loss of “atrial contribution” results in 5–15% cardiac output reduction, especially in patients with decreased ventricular compliance. Due to high HR diastole decreases resulting in the reduced ventricular filling. R–R interval variations result in the heart force change that frequently leads to deficiency pulse. The above mentioned changes result in arrhythmogenic cardiomyopathy manifesting in progressive LA cavity dilatation, myocardial contractility decrease, etc [3, 4].

Thromboembolitic complication is one more effect of irregularity and chaotic nature of the atrial myocardial areas. The most frequent thrombosis location is the left atrial auricle, its anatomic features contributing to it — a cone-shaped form, irregular internal surface. AF results in LA cavity dilatation, contractility suffers leading to slow blood flow in LA auricle. In addition, blood clotting system in AF patients activates, and endothelial function disturbs [3, 4].

In most cases AF clinically begins with short and rare episodes, which eventually become longer and more frequent. Clinical progression depends on contributing factors. Patients often have asymptomatic AF episodes even in the presence of clinically evident AF. First AF signs can be such complications as ischemic stroke or tachyarrhythmic cardiomyopathy. In natural course, paroxysmal AF becomes persistent then developing into permanent [3, 4].

In the presence of such a “triggering factor” as mitral valve disease, AF progression depends on the defect intensity. AF episodes clinically worsen the course of heart defects, promote the increase of heart failure sings, the number of complications including thromboembolisms. Compensatory mechanisms suppressing the signs of mitral valve disease in such patients terminate contributing to significant progression of chronic heart failure [17].

Evolution of atrial fibrillation treatment modalities

The first surgical procedure developed specially for AF treatment and described in 1980 by J. Cox consisted in LA isolation and aimed at SR restoration in the rest part of the heart. This approach corrected two of three disturbances in AF: irregular heart contractions and impaired hemodynamics, though thromboembolism risk remained high, since LA continued fibrillating. This procedure was used in rare cases and did not have wide spread occurrence [1, 37].

In 1985 G. Guiraudon developed a new procedure “Corridor” consisting in an isolated myocardial zone formed between a sinoatrial and atrioventricular node. The procedure corrected irregular heart contractions related to AF, but both atria had their own fibrillation rhythm, therefore there was no effect on thromboembolism risk and decreased hemodynamics [1, 38].

Further development of J. Cox surgical techniques affecting AF in laboratory resulted in the introduction of “Cox-Maze I” procedure in 1991. It consisted in incisions made on the left and the right atrium deep through the wall followed by suturing that caused scar formation, and the scar was the only possible pathway for excitation pulses in atria with isolation of macro-reentry circles [1, 24]. This operation enabled to obviate AF effectively, though had some disadvantages: sick sinus syndrome, high frequency of LA dysfunction, the increase in pacemaker implantation rate [23, 37]. “Cox-Maze I” procedure had the same problems. In addition, it required superior vena cava transection and later was rejected as technically sophisticated. A surgical technique was modified and a final variant was brought forward — “Cox Maze III”, which later was recognized as “a gold standard” (Fig. 2). The efficiency of this procedure in a long-term period is 89–97%, though its application is restricted by an operation duration, labor

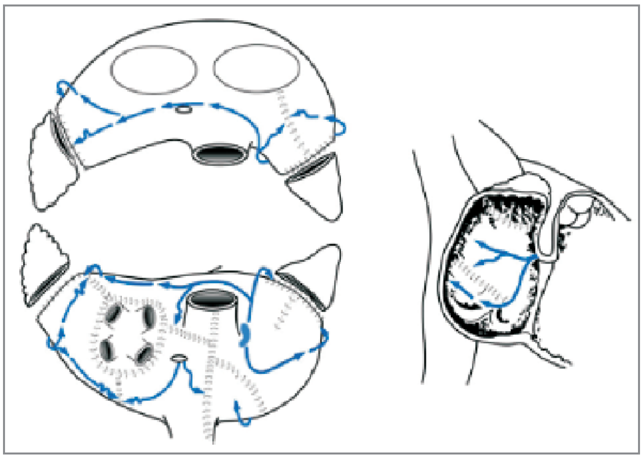

Fig. 2. “Cox-Maze III” procedure [14]

intensity, a high qualification level of a surgeon [37–43].

The complexity of a large-scale implementation of “Cox-Maze” operation made researchers develop modifications simplifying the procedure and reducing the period of artificial circulation and complication rate. It became possible with a wide range of ablation (destruction) devices using various kinds of energy, which replaced a part or all incisions of the initial operation [37, 41, 44–46]. A key point of their application is the efficiency in safe transmural damage formation to prevent an impulse from breaking resulting in recurrent AF. An ideal energy source and a device should provide transmurality, not cause damage of the surrounding structures, and provide the effect quickness, have compact construction, good manageability. Currently, cardiac surgeons have the following techniques: cryoablation, microwave ablation, ultrasound and radiofrequency ablation [1, 2, 23, 45].

In *cryoablation*, in contrast to other methods, ablation results from freezing, not heating. The use of nitric oxide or argon provides significant transmurality effect on a stopped heart and minimum collateral damage preserving the tissue collagen structure [1, 47]. However, the technique is not to be used on a working heart since a required temperature is not reached due to tissue warming up by circulating blood.

A mechanism of *microwave ablation* consists in myocardial heating by the oscillations of water molecules in tissue caused by microwaves. The extent of damage depends on type of a device used, the efficiency being 70 to 90% [1, 48].

The ablation using *high-frequency ultrasound* enables to form noncontact extensive lesion with no effect on surrounding tissues [1, 36]. Currently, there are used devices with ultrasound frequency 1–5 MHz and higher forming focused damage due to prompt myocardial heating up to 80°C. The main advantages of this technique are the possibility to focus ablation on the selected depth and direct heating of tissue “in bulk”, in consequence of which of heat-transport effect of circulating blood reduces. However, according to some researchers, the result is not always achieved due to fixed depth of damage that creates a problem in case of pathologically thickened atrial tissues. Moreover, the devices are rather large and costly [1, 36].

Radiofrequency ablation characteristics

Radiofrequency ablation (RFA) is a medical procedure consisting in the damage of body tissues by heating due to generated heat resulted from high-frequency oscillations of electrical field — 50 kHz to 1 MHz [38, 42]. The technique is widely used in various medical fields, where it is necessary to apply dosing damage of organ and tissue area — cardiovascular surgery, oncology, etc. Modern RFA devices enable to control the extent and depth of damage, and perform both direct and mini-invasive procedures [42].

RFA for arrhythmia treatment was put into practice over 15 years ago. Due to its characteristics the method enables to succeed in damaging myocardial area and, subsequently, pulse generation and conduction. RFA enables to “break” macro-reentry circles and suppress focus activity, providing dosing and controlled myocardial damage recovering normal pulse conduction along atrial and ventricular myocardium that found its application in such pathologies as atrioventricular reciprocating tachycardias, atrial and ventricular ectopias.

RFA application in AF management. Currently, RFA has spread widely and is used to treat both “isolated” AF, and one-stage AF correction in cardiac surgery under artificial circulation [42]. This kind of energy was one of the first, which was used intraoperatively to substitute “cut-and-sew” technique. Monopolar electrodes initially introduced into practice proved their efficiency in forming endocardial injuries in most cases, but there were difficulties when applied epicardially on a working heart. Moreover, as in the case of using some other energy sources, in monopolar ablation the devices radiate unfocused heat causing collateral damage in careless usage. Complications occurring in the operation of monopolar devices include the damage of coronary arteries, cerebrovascular disease, phrenic nerve injury, and the most threatening — esophageal perforation with atrioesophageal fistula formation [1, 37, 41].

To prevent possible complications and overcome RFA restrictions, there were developed the devices for bipolar ablation. The clamps for bipolar RFA are separated from circulating blood effect, and enable to perform quicker ablation with a limited collateral damage. Animal tests have proved the technique to be able form transmural injuries on a working heart for a short period of time, and a wide clinical experience in its application has proved the absence of collateral damage [1].

AF RFA application in patients with mitral valve diseases. The possibility and necessity of AF surgical management application in patients with mitral valve diseases during the operations using artificial circulation is shown by many researchers [24, 28, 29, 32, 35, 40, 47, 49–54]. The authors mention the operation to result in survival increase, reduced number of thromboembolic complications, though there is other information [25, 55]. As early as in the 90s, when “Cox-Maze” operation was introduced, the use of one-stage procedures affecting atrial myocardium according to “cut-and-sew” technique demonstrated high frequency of SR restoration in patients with mitral valve diseases including those with rheumatic etiology [49]. The most part of patients (75–90%) were managed to recover regular rhythm, and restore LA transport function, atrioventricular synchronization having reduced the risk of thromboembolic complications. The complexity of an operation prevented it from widespread use; however, it remained being in use in a number of centers until recently in various modifications [56].

At the beginning of the XXI century the appearance of monopolar RFA enabled to simplify "Cox-Maze" procedure, though its efficiency turned out to be lower — about 70%. The results were more successful in patients without atriomegaly (about 88%) [57, 58]. Significantly reduced additional time for artificial circulation required for this combined procedure made radiofrequency modification more popular, and subsequent appearance of bipolar ablation enabled to equal RFA efficiency with a classic "Cox-Maze" method [39, 40, 59]. It should be noted, that "Cox-Maze IV" technique requires the application of separate left- and right atrial incisions that is difficult in patients, who has undergone cardiac operations before, and in some cases places certain restrictions on MV imaging. For this reason, as well as for operation volume reduction, some authors have suggested the variants of mono-atrial ablation [46, 24, 54, 60–62, 63]. In particular, as early as in the 90s of the XX century there was proposed a theory of LA "critical mass" significant for AF maintenance; and in this regard there were suggested different variants of LA reduction [64].

Conclusion. Currently, the question of optimal management of patients with atrial fibrillation both as a separate pathology and in combination with other heart diseases still remains open. Surgical correction of mitral valve diseases enables to gain access to atrial tissue areas, which play a key role in the occurrence and maintenance of this type of arrhythmia in electrophysiological terms. It is worth mentioning that the interest in the study of atrial electroactivation by epicardial mapping has been rekindled, and it is likely to update the data on fibrillation mechanisms and improve the efficiency of its management. A critical goal requiring new researches is to determine an adequate modality able to affect atrial tissues, sufficient and safe operation volume, which would enable to obtain an optimal result with minimum complications and introduce this technique into practice.

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