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Mitral Valve Prolapse in Pregnancy: Modern Concept

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Additional information is available at the end of the chapter

Abstract

This chapter presents the recent literature data data on the problems of etiopathogenesis, cardiac, and obstetric risk of mitral valve prolapsus, as well as the tactics of patients with this pathology. Modern views on the role of genomic, genetic disorders, and metabolomics in violations valvular structures in the etiology and pathogenesis of clinical manifestations of the mitral valve prolapsus. In addition, the data on the peculiarities of pregnancy and childbirth in women with mitral valve prolapsus (miscarriage, cervical incompetence, preeclampsia, fetal growth restriction, placental insufficiency, labor anomaly, and postpartum hemorrhage) are studied. However, ambiguous and sometimes conflicting data on the relationship and the incidence of these complications with mitral valve prolapsus require further research to determine the set of diagnostic and preventive measures.

Keywords: mitral valve prolapse, mitral regurgitation, mitral valve prolapsus classification, diagnostic imaging techniques, preeclampsia, anomalies of labor activity

1. Introduction

In recent years, the importance of extragenital pathology in severe maternal morbidity and mortality has increased significantly worldwide [1–3]. The role of diseases of the cardiovascular system in the complications of pregnancy and the frequency of perinatal complications are increasing [4, 5]. In addition, often in the genesis of diseases of internal organs in a pregnant woman is the genetic conditioned systemic disorders of histogenesis, in particular connective

tissue dysplasia [5–7]. The prolapse of the mitral valve is one of the most common and studied visceral manifestations of connective tissue dysplasia (CTD). Connective tissue dysplasia (DST) is the disorder of the connective tissue of polygenic multifactorial nature, combined into phenotypes on the basis of the commonness of external and/or visceral features [6]. CTD is characterized by defects in fibrous structures and the basic substance, leading to a disorder of homeostasis at the tissue, organ, and organism levels in the form of various morphofunctional disturbances of visceral and locomotor organs.

Interest in the study of MVP is due primarily to its relatively high frequency in the general population and among young women of reproductive age, as well as possible complications—sudden death, arrhythmias and congestive disorders of the heart, infectious endocarditis, and thromboembolic disorders. However, previously reported MVP complications such as stroke, disautonomy (postural orthostatic tachycardia syndrome (POTS)), panic attacks, feelings of fear, and transient ischemic attacks [8] are not currently considered in connection with the MVP itself [9]. In the majority of women, no cardiovascular pathology has been detected in 10 years after the diagnosis of MVP [3].

2. Definition

Primary mitral valve prolapsus (MVP) related to small (minor) cardiac abnormalities (MCA) is considered to be one of the most common heart valve anomalies. Mitral valve prolapsus (MVP) represents a range of valvular abnormalities that allow one or both mitral valve leaflets to extend above the plane that separates the atria and the ventricle.

MVP is such a pathology of the valve apparatus (some redundancy of it), in which one or both mitral valve flaps bend ("sag," prolapse) upward and posteriorly above the plane separating the atria and ventricles (above the valvular ring plane) during systole [10–12]. The valves can remain connected or can be separated, which leads to a different degree of regurgitation (**Figure 1**).

The more pronounced prolapse can be caused by myxomatous degeneration of mitral valve flaps. An anomaly of the mitral valve may be an isolated visceral manifestation of CTD, but it can also be a part of dysplastic syndromes. MVP (and sometimes the tricuspid valve prolapse) can be associated with other intracardiac anomalies, in particular, an interstitial septal defect [3, 5].

The average frequency of MVP in the population is 3–10% with a widespread frequency according to literature data, depending on population factors (gender, age, race) [6, 13, 14], as well as the diagnostic method and diagnostic criteria [10, 11].

Individuals with classic MVP (leaflet thickness of ≥5 mm; 1.3%) and non-classic MVP (leaflet thickness of <5 mm; 1.1%) had similar age and sex distributions. MVP prevalence was similar in three ethnic groups (2.7% in South Asian, 3.1% in European, and 2.2% in Chinese) [10]. MVP patients were leaner and had a greater degree of mitral regurgitation (MR) than the general population [6, 7]. MVP may be slightly more common in women than in men. The
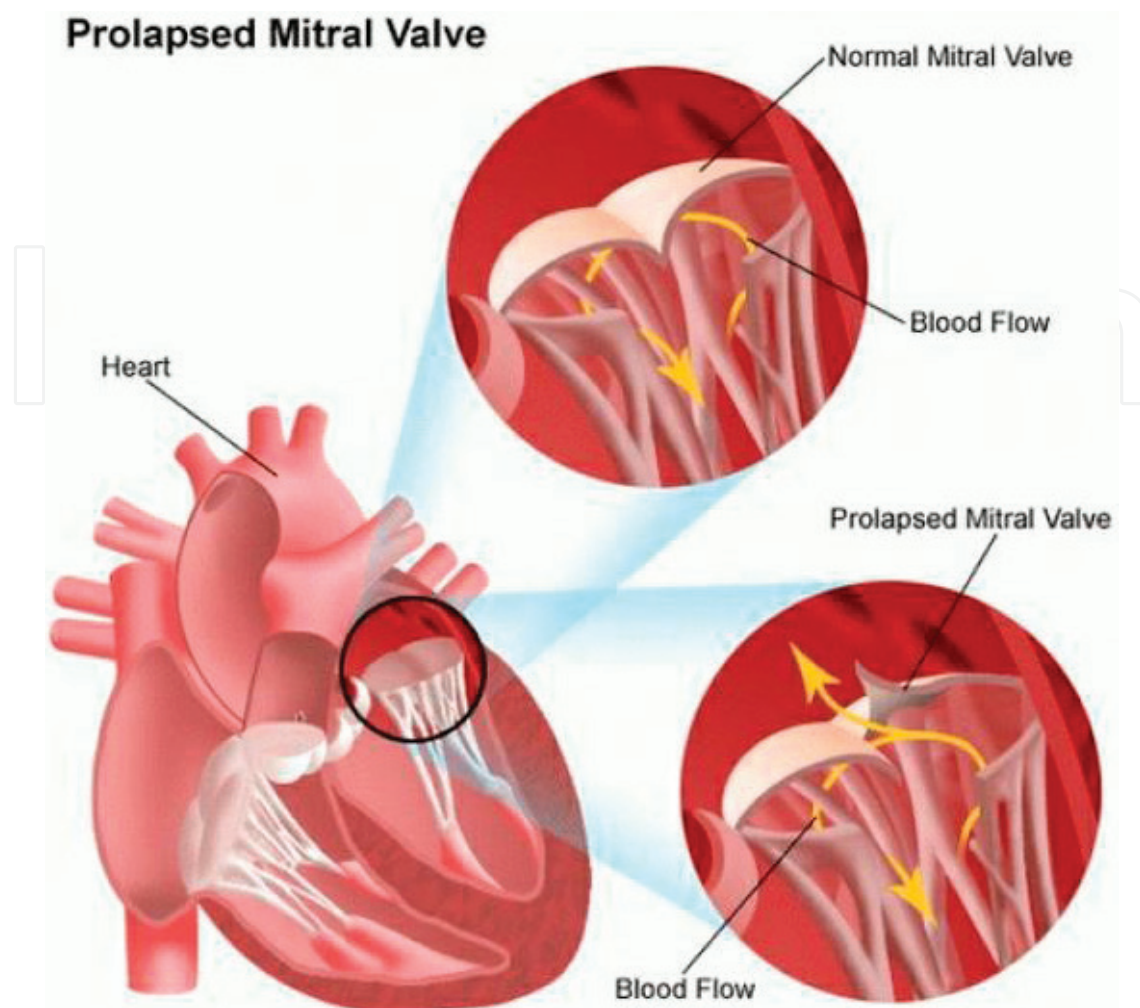
Figure 1. Mitral valve prolapse.

majority of patients with MVP have mitral regurgitation (MR), but most patients with MVP (approximately 75%) have mild, trace, or no MR [1]. Severe MR is uncommon, identified in 4% of patients with MVP. Unlike adults, mitral valvulopathy (MVP) with Marfan syndrome in newborns can be accompanied by severe regurgitation and functional disorders of the contractile activity of the heart leading to congestive heart failure [15]. Most often among all population groups (17–38%), MVP is noted in women of reproductive age [10, 16]. According to the REPLICA study (mitral valve prolapse prevalence among young people), MVP is detected more often—in 4.3% of cases [17].

Therapists working in obstetrics consider MVP the most common heart anomaly in pregnant women [18]. The proportion of MVP in the structure of small heart anomalies in pregnant women is 60.8% [19]. In the recent past, this pathology was considered to be so frequent, especially among young women, that a number of authors proposed to consider MVP as a variant of the normal structure of the mitral valve [20]. However, the standardization of echocardiographic criteria and a better understanding of the structure of the valvular apparatus led to a significant decrease in the frequency of the detection of true MVP, which is 0.5–3.0% in the population and 1% in women of all age groups with a maximum frequency—in reproductive age. A large

retrospective study, during which 16,185 echocardiograms were analyzed, performed according to clinical indications in the Consultative-Diagnostic Center of National Medical Research Center of V.A. Almazov (St. Petersburg, Russia) from 2008 to 2011, also showed a low prevalence of MVP and in the Russian population—1.3% [21].

3. Classification

For the first time, mitral valve prolapse was described by J.B. Barlow et al. in 1963.

There are multiple ways of classifying MVP, underscoring the heterogeneity of this disorder:

- Etiologically, MVP is classified as primary (degenerative disease in the absence of identifiable connective tissue disease, sporadic, or familial) versus secondary MVP (associated with an identifiable disorder such as Marfan syndrome).

- Clinically, MVP can be classified as syndromic when extracardiac manifestations are present (e.g., pectus excavatum) versus non-syndromic, isolated MVP.

- MVP is also classified by the severity of the abnormal movement of the valve. The leaflets are described as billowing when the tips of leaflets remain in the left ventricle (LV) versus flail when the tip(s) of one (or both) leaflets prolapses into the left atrium (LA).

- Morphologically, MVP is classified as classic (also known as Barlow's syndrome with markedly and diffusely thickened leaflets (≥5 mm) with bileaflet prolapse) versus non-classic (with limited or absent thickening (thickness <5 mm) and segmental prolapse).

- Doppler echocardiography can also distinguish MVP without mitral regurgitation (MR) from MVP with MR.

The 2014 American Heart Association/American College of Cardiology guidelines for the management of patients with valvular heart disease separate mitral regurgitation by a mechanism into primary (disease of one or more valve components including leaflets, chordae tendineae, papillary muscles, or annulus) and secondary (disease of the left ventricle) [22]. In this classification, primary disease includes all forms of MVP along with other causes of MR involving the components of the valve (e.g., calcific degeneration, cleft mitral valve, leaflet perforations, etc.). Isolate primary (congenital, idiopathic) and secondary prolapse develops against the background of the already existing diseases of the cardiovascular system. Primary prolapse of the mitral valve is a hereditary violation of the formation of the connective tissue [6, 7, 10, 11]. It should be noted that in the MVP structure, the primary occurs much more often. The share of the secondary accounts for only 5% of the total number of observations. Clinically anatomically, MVP is a syndrome that accompanies many nosological forms [10, 15, 16].

Currently, there are several MVP variants [23]:

1. pleiotropic manifestation of some classified hereditary disorders of the connective tissue (syndromes Marfan, Ehlers-Danlo, etc.). Thus, the combination of MVP with aortic

dilatation and signs of connective tissue dysplasia of seven or more points gives reason to consider it as associated with the Marfan syndrome. However, it should be emphasized that only 1–2% of patients with MVP have one of the monogenic undifferentiated disorders of the connective tissue [6];

2. independent clinically and prognostically significant syndrome: primary familial mitral valve prolapse (MIM 157700), primary myxomatous mitral valve prolapse (MIM 607829 or 610,840). In the absence of signs of one of the monogenic NNST, in the case of detection of MVP with hemodynamically significant mitral regurgitation and/or myxomatous degeneration of the valves in persons with a young age, it is possible to speak with a high probability of the presence of a clinically significant primary MVP. To diagnose genetically determined primary MVP, it is not possible to restrict only echocardiography to a study, but it is necessary to take into account the results of a family survey, the phenotypic data, and the clinical picture of the disease. For evaluation of MVP, its combination with the signs of dysplasia of the connective tissue or the absence thereof is also important. The combination of MVP with clinical symptomatics allows talking about the syndrome of MVP. It is characterized by vegetative dysfunction, arterial hypotension and orthostatic failure, cardiac rhythm disturbances, and repolarization disorders on the ECG [6];

3. the minor heart anomaly, often accompanying other classified and unclassified dysplastic syndromes.

With the exclusion of MVP syndrome, prolapse of the valves without their thickening and significant mitral regurgitation can be regarded as one of the variants of a small heart anomaly, the number of which, as is well known, closely correlates with the number of external signs of dysembryogenesis detected [24].

4. Etiopathogenesis

To explain the causes of primary prolapse of the mitral valve, several theories have been proposed. Proponents of the "myocardial" theory in the histological study of the myocardium found interstitial fibrosis and hypertrophy of myofibrils in patients with mitral valve prolapse and in electron microscopy—degenerative changes in mitochondria, endocardium thickening [25, 26].

The revealed changes allowed to make an assumption about the similarity of morphological changes with mitral valve prolapse and dilated cardiomyopathy. However, after conducting a complex echocardiographic, radionuclide, and angiographic study, the hypothesis of the cardiomyopathic etiology of the primary prolapse of the mitral valve has not been confirm [6, 26]. The theory of the "rheumatic" nature of the prolapse of the mitral valve was also common. This point of view is confirmed by information about a greater frequency of prolapse in patients with rheumatism. Supporters of this theory explained the mechanism of prolapse of the valves with partial chord separation as a result of inflammatory changes in the endocardium [5, 27]. There are also data indicating the possible involvement of a viral infection in the

development and progression of mitral valve prolapse [28]. However, modern protocols for management of patients with MVP do not provide for antibiotic prophylaxis [3].

At the basis of the development of secondary MVP lies the violation of myocardial contractility of the left ventricle and dysfunction of the papillary muscles. It develops under the following pathological conditions: inflammatory processes (myocarditis), cardiomyopathy, myocardial dystrophy [10, 16], ischemic heart disease, a decrease in tissue elasticity as a result of left ventricular contraction asymmetry and papillary muscle ischemia and tendon chords, violation of autonomic innervation and impulse conduction in myocarditis, extrasystole, WPW syndrome, with neuroses and hysteria. Also, the cause of secondary MVP can serve as a blunt trauma to the heart [22].

Most researchers are supporters of the "valve" theory. This theory presupposes the presence of a genetically determined collagen defect, which leads to the "weakness" of the connective tissue of the mitral valve flaps and their prolapse into the atrial cavity. Three gene loci are described on 16, 11, and 13 chromosomes, but the genetic defects underlying them are not known to date. The recessive form of MVP associated with the X chromosome is known as myxomatous dystrophy of the heart valves, and mutations of the gene for the pathogen have recently been identified [6].

There are several possible pathogenetic mechanisms that can explain the onset of MVP. According to some data, the role of magnesium deficiency in the development of MVP is great. The lack of magnesium reduces the activity of magnesium-dependent adenylate cyclase, which ensures the removal of defective collagen [29] and affects the ability of fibroblasts to produce collagen [16]. In addition to the direct participation of magnesium ions in the processes of collagen formation, the role of magnesium in the functioning of the vegetative nervous system is undoubtedly important, since a deficiency of magnesium ions promotes an increase in the level of catecholamines of the blood plasma, that is, the development of hypercatecholaminemia, changes in the tone of the papillary muscles, and the formation of MVP.

5. Clinical picture

Symptoms attributed to mitral valve prolapsus (MVP) cannot clearly be explained by the degree of prolapse or mitral regurgitation. However, autonomic or neuroendocrine dysfunction has been suggested as a possible cause of the nonspecific symptoms in many patients with MVP. Patients with MVP tend to exhibit the following findings when compared to controls [3, 4]:

- elevated urine and plasma catecholamine levels;

- an exaggerated heart rate response to phenylephrine;

- a less than expected bradycardiac response to the dive reflex;

- the reproduction of symptoms with isoproterenol infusion.

The specificity of these findings for MVP is uncertain. One study found a series of abnormalities in patients with symptoms of autonomic dysfunction, which did not correlate with the presence or absence of MVP [5].

An association between panic disorder and MVP has also been suggested by several studies, including a meta-analysis [6]. However, these studies have been criticized because of inconsistencies in the diagnostic criteria used for both panic disorder and MVP and the use of imperfectly matched controls. In addition, panic disorder and MVP are both common illnesses with similar age and gender distributions, suggesting that their association may only be a coincidence.

The clinical manifestations of prolapsus of the mitral valve differ in variety [5, 6]. At the same time, most researchers note the polymorphism of the clinical picture [3, 17]. Data on the frequency of clinical symptoms and the pathogenetic mechanisms of their formation are contradictory [3, 10, 11, 13]. However, the recognition of prolapsus is accompanied by a fairly clear and definite clinical picture. It is proposed to isolate clinically and morphologically significant MVP syndromes:

1. the pain syndrome in the left half of the chest (32.3–65%) [6, 10, 17]. At the same time, the mechanisms of the formation of the pain syndrome remain controversial. Currently, the most common explanations of pathogenetic mechanisms of pain syndrome are local myocardial ischemia as a result of tension of papillary muscles, microthrombemia in the zone located between the left atrium and the back wall of the mitral valve, a decrease in the diastole duration as a result of an increase in the heart rate, and sinus tachycardia in response to stress or physical exertion [3];

2. the syndrome of disturbance of vegetative regulation of heart rhythm (25.8–79%). The complaints about the heartbeat and interruptions in the work of the heart are noted in individuals in cases [30]. There was no consensus on the mechanism of cardiac rhythm disturbance and repolarization process disturbances in these patients, the role of abnormal traction of papillary muscles, the presence of late ventricular potentials, myxomatous degeneration of dilated valves, and dysfunction of the autonomic nervous system was discussed [10, 17];

3. the hyperventilation syndrome (dyspnea—15.6–31.5%). Domestic authors with mitral valve prolapse noted the presence of a feeling of lack of air and obstacles in the way of inhaled air, the need to periodically make deep sighs, and a feeling of dissatisfaction with inspiration [6]. The main pathogenetic mechanism is disautonomy [10];

4. the hemorrhagic syndrome: nasal bleeding, tendency to easy formation of bruises, bleeding gums, prolonged bleeding after removal of the teeth, prolonged and (or) profuse menstruation. The tendency to easy bruising and nasal bleeding can be explained by the presence of disturbances in the hemostasis system in patients with MVP—a change in the aggregation function of platelets, a decrease in the activity of von Willebrand factor in the blood plasma, and a disruption of the final stage of blood coagulation [31]. As is known, hemorrhagic syndrome is one of the manifestations of mesenchymal dysplasia, which explains its presence in patients with prolapse of the mitral valve;

5. the vascular disorders in the limbs of persons with mitral valve prolapse (68.8%), which are presented in the form of vascular necklace, Raynaud's syndrome, changes in the color of the limbs, idiopathic pastosity, or swelling [6]. Lipothymia is a complex of sensations that preceded the loss of consciousness noted in the work of T.M. Dominitskaya (1998) in 69.0% of patients with mitral valve prolapse in combination with abnormally located chord and in 51.0% of persons with abnormally located chord with orthostatic load, emotional stress, prolonged stay in a vertical position, and in stuffy rooms [32];

6. the vegetative crises (sympathetic-adrenal, vago-insular, mixed). These are the most striking manifestations of MVP;

7. the mental disorders: neurasthenia, anxiety disorders, anxiety-phobic disorders, mood disorders. When assessing the results of a comprehensive psychological examination, it was found that in persons with mitral valve prolapse, there are a number of distinguishing features from healthy people: inadequate self-esteem (32.1%), low level and inadequacy of attitudes (50.9%), high situational anxiety (32.7%), low emotional stability (39.0%), and a decrease in the dynamic indicators of mental activity [6].

Along with the widespread point of view about the propensity of patients with mitral valve prolapse to hypotension, recently there have been isolated reports of the presence of arterial hypertension in patients with prolapse of the mitral valve [5]. The possibility of hereditary predisposition to arterial hypertension, mixed with hereditary pathology of connective tissue, is not excluded.

However, not all authors agree with the presence of MPV syndrome with the above-described clinical symptoms [3], believing that PMC is only an anatomical feature of the valve structure, if it is not a manifestation of the Martha syndrome. Clinical manifestations of approximately equal frequency are observed in women with and without EchoCG signs of MPV.

6. Diagnostics

It should be emphasized that the main method of diagnosis of mitral valve prolapse is currently two-dimensional echocardiography. However, certainly, it is necessary to take into account the history of the patient, including the family history, the presence of concomitant markers of connective tissue dysplasia, the presence of clinical manifestations of prolapse MV, including relatives, clarify the family thrombotic anamnesis or the presence of sudden deaths in relatives.

In most cases, the diagnosis of prolapse MV in pregnant women is established even before its onset. However, in a part of young primitive women—MVP—a random echocardiographic finding requires a careful evaluation of clinical and anamnestic risk factors in each pregnant woman [5, 33].

6.1. Cardiac examination

The most common auscultatory features of mitral valve prolapse are the non-ejection click (single or multiple) and the murmur of mitral regurgitation. The click is thought to be caused by snapping of the mitral chordae during systole when the valve bows into the atrium. The click is mobile, meaning its timing varies with maneuvers that change the left ventricular volume, occurring earlier in systole with sitting, standing, or other interventions that reduce ventricular size, or later with those interventions that increase the chamber size such as squatting (movie 4 and movie 5) [34]. An MVP click should be differentiated from the aortic or

pulmonary ejection clicks (occurring early in systole, at the foot of the carotid upstroke) and from other cardiac sounds (split first or second heart sounds, pericardial sounds, atrial septal aneurysm clicks).

With a routine clinical examination and auscultation of cardiac tones, a systolic click is heard between the I and II heart tones, together or without middle diastolic or late systolic murmur, which is a characteristic symptom. The presence of these auscultative data may vary depending on the position of the body of the pregnant woman or the degree of her hydration. Similar auscultative changes can occur in healthy women during pregnancy, varying in the time of click occurrence and in mitigating or shortening the time of noise, and when series of echocardiographic studies in the presence of MPV in some women EchoCG signs of it disappear [6].

6.2. Diagnostic imaging techniques

In most pregnant women who do not show any other clinical signs, so in the absence of significant regurgitation in *echocardiography*, women should talk about the safety of pregnancy and childbirth, as well as the absence of a negative effect on the fetus of this condition [3]. MVP is diagnosed at the maximum systolic displacement of the mitral valve flaps beyond the ring line in the parasternal longitudinal position by more than 2 mm. The use of the parasternal longitudinal section for the diagnosis of MVP is due to the peculiarities of the shape of the mitral valve ring, while the isolated displacement of the anterior valve beyond the ring line seen in the four-chamber apex position is the main cause of its overdiagnosis. In echocardiographic conclusion, it is necessary to indicate the depth of prolapse, the length and thickness of each of the valves, and the degree of mitral regurgitation [6, 12] (**Figure 2**).

The normal length of the front leaf is 21–24 mm, the rear is 12–14 mm. Depending on the thickness of the leaf, the classic MPV is distinguished, with a valve thickness of more than 5 mm in diastole (reflects the presence of myxomatous degeneration of the valves) and nonclassical MPV—with a thickness of less than 5 mm.

The determination of the degree of mitral regurgitation is currently conducted according to the recommendations of the ANA/ACC [6]. For this purpose, the following qualitative indices are used: the diameter of the vein of the regurgitation jet (vena contracta), the volume of regurgitation, and the area of the regurgitation opening calculated according to the area of the proximal equal-velocity surface (PISA). Specific for MPV is the mitral regurgitation that occurs at the end of the systole; it is usually high speed and eccentric.

The evaluation of LV systolic function is also an important component of EchoCG study. It is an important prognostic factor in patients with MVP and severe MH [6, 12]. There is evidence of worsening of LV systolic function in young patients with MVP and without significant mitral regurgitation [35].

The development of 3D technology, especially real-time 3D-TEE, provides excellent rendering of the mitral valve complex. Live 3D-TEE has become routine in pre/intraoperative imaging of the mitral valve and in percutaneous mitral valve interventions. 3D-TEE efficiently identifies
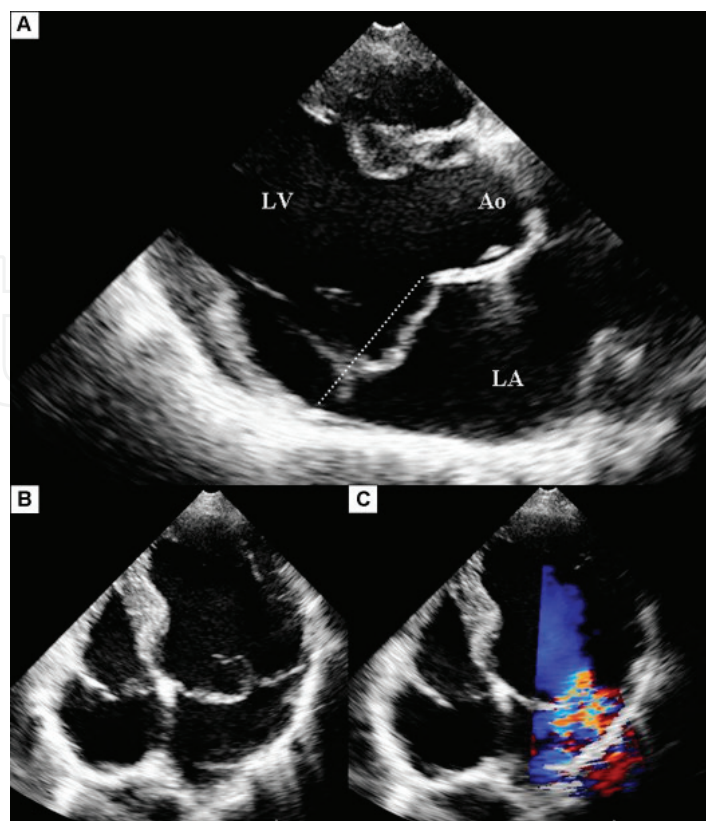
Figure 2. Echocardiography in mitral valve prolapse.

correct location of prolapse and flail segments, and by reconstruction of the 3D image from the left atrial view (surgical view), information is easily communicated to the surgical team. In a study comparing 2D TEE with 3D-TEE, both expert and less experienced echocardiographers more accurately described the mitral valve pathology using 3D-TEE (with surgical pathology as the reference), with less experienced interpreters gaining a significantly greater advantage from using 3D-TEE [36]. 3D-TEE is the key imaging modality for guidance of percutaneous mitral valve repair with the MitraClip system.

With increased use of 3D-TEE, cleft-like indentations of the posterior mitral leaflet are more frequently recognized and may be present in up to one-third of patients with myxomatous MVP [36]. Appropriate recognition of cleft-like indentation is important when planning surgical or percutaneous mitral valve repair. However, it must be emphasized that not all cleft-like indentations apparent on 3D reconstruction are associated with mitral regurgitation (i.e., many are "non-functional" clefts, being visible only during diastole, which do not require a repair). The best approach to determine the significance of cleft-like indentation is to examine the mitral valve anatomy from the left ventricular en-face view, in both 3D and 3D color.

3D-TEE also allows insights into the dynamic mitral annulus function, with early-systolic area contraction and saddle-shape deepening contributing to mitral competency. The mitral annulus in MVP is also dynamic but considerably different from normal patients, with loss of early-systolic area contraction and diminished saddle-shape deepening despite similar magnitude of ventricular contraction, suggestive of ventricular-annular decoupling [36]. With the rapid development of percutaneous interventions for mitral regurgitation, accurate

assessment of the mitral valve anatomy (annulus area and perimeter, inter-commissural and septal-lateral diameters) becomes increasingly important. These can be reliably measured by both 3D echocardiography and computed tomography (CT).

While 2D and 3D imaging techniques allow identification of anatomical substrate, Doppler echocardiographic techniques are key to estimating the severity of MR. The criteria used to diagnose severe MR are discussed separately.

MR severity should be quantitated in all patients with a visual appearance of greater than mild MR on color Doppler. Formal quantification of mitral valve severity not only minimizes errors intrinsic to color Doppler visual quantification of severity but also provides essential information about a patient's individual risk. Quantitative measures of MR (regurgitant volume and orifice) are essential predictors of outcome [36] as confirmed in two independent prospective studies totaling more than 1000 patients followed long term.

In a dynamic echocardiographic study in pregnant women with prolapse of the mitral valve of women, there are stable sizes of the left chambers of the heart, as well as the thickness of the left ventricular myocardium and the interventricular septum throughout the period of pregnancy and in the postpartum period [5]. With an increase in the period of pregnancy from the first to third trimester, there is a natural increase in the frequency of a greater degree of prolapse of the mitral valve and to a lesser extent the degree of mitral regurgitation.

In accordance with the generally accepted approaches, the stratification of the risk of cardiovascular complications and death in patients with MVP should be based, first of all, on the evaluation of the severity of mitral regurgitation and the thickness of the mitral valve leaf [5, 6, 33]. The latter characterizes the presence and severity of their myxomatous degeneration. With a leaf thickness of 5 mm or more, the total probability of sudden death, endocarditis, and cerebral embolism, the likelihood of developing mitral insufficiency, rupture of chords, and ventricular arrhythmias in such patients can be attributed to the high-risk group [6, 10, 12, 13, 37].

The degree of risk was determined in the presence and severity of a number of factors: the auscultatory pattern, the degree of prolapse, the severity of myxomatic degeneration of the valves, mitral regurgitation, age, fibrillation of pre-arthies, chronic heart failure, hypertension, and others [38].

Most patients with MVP, without signs of MR and mild MR, can be classified as low risk with a favorable prognosis [3, 10, 15]. Life expectancy at them corresponds to that in the general population [20]. The unfavorable course of MVP is the increase in MR, leading to dilatation of the LV and LP, development of atrial fibrillation, LV systolic dysfunction, and chronic heart failure. The onset and rapid progression of MP may be due to the rupture of myxomatologically altered chords [6].

The presence of altered valves with MVP increases the risk of infectious endocarditis, although overall its probability in the population of patients with MVP is low [39]. Thromboembolism of cerebral vessels is the main cause of neurologic symptoms (transient ischemic attacks and strokes) in patients with MVP, and the risk of embolism is higher than in the general population [3, 6, 10]. Sudden death is a rare complication of primary MVP (less than 2% of cases with prolonged follow-up, with an annual mortality of less than 1%). The main cause of sudden

cardiac death in MVP is ventricular tachyarrhythmias, which are especially common in family MVP forms [3, 10]. In a number of cases in the presence of pain in the left half of the chest, in women, there is an inversion of the T-wave on the ECG, especially in the II and III thoracic leads, even in the presence of normal coronary angiography. When conducting a treadmill test, it is also possible to detect the depression of the ST segment, indistinguishable from that of myocardial ischemia.

7. Mitral valve prolapsus and pregnancy

The features of the course of pregnancy and childbirth in women with DST are not sufficiently studied. Pathology of pregnancy is much more common in women with MVP and CTD than in healthy women—85.5 versus 53.3%. The threat of spontaneous abortion and miscarriage occurs in 50% of women with MVP, and the threat of premature birth is observed six times more often than in healthy pregnant women [13]. The main reason for the habitual miscarriage of pregnancy in this group of patients is cervical insufficiency [16]. In women with MVP and CTD, the threat of interruption of pregnancy up to 20 weeks is in almost one-third of cases, the threat of premature birth—in 17.2%, pregnancy ended in premature births of 4.6% [40]. The threat of spontaneous termination of pregnancy in the first trimester was noted in every third patient with MVP, in the II trimester—in 25.9% of patients with MVP; in the third trimester—in 15.5% [33]. The 9.6% of women with habitual miscarriage have MVP [41, 42].

The pregnancy in patients with MVP and undifferentiated connective tissue dysplasia is accompanied by an increase in the frequency of the threat of interruption in the first trimester of pregnancy—OR 1.7, hyperemesis gravidarum—OR 1.8, the threat of interruption in the second trimester of pregnancy—2.5%, premature births—OR 3.2, and polyhydramnios—OR 2.7. The course of labor is complicated by cervical rupture—OR 1.8 and weakness of labor activity—OR 3.7 [7].

The most common complication of the second half of pregnancy in women with MVP is preeclampsia—51.7% [16, 43], and the course of labor in these patients is characterized by frequent complications [16, 40, 43]. It is known that preeclampsia ranks two to three in the structure of causes of maternal mortality [33, 44–47] and is one of the main causes of premature birth and perinatal fetal death. Every fifth child born to a mother with preeclampsia, to some extent, deviations in physical and psycho-emotional development are observed [7].

Another complication, no less important for obstetrics—preterm rupture of placental membranes and outflow of amniotic fluid—in women with MVP is observed in 40.0–51.6% of cases [7, 29, 43, 48]. The frequency of premature and early outflow of amniotic fluid in pregnant women with MVP is 38.1%.

Among the characteristics of the course of labor associated with MVP, the relationship with the rapid course of labor is described, and with a severe degree of MVP, the rate of fast and rapid delivery in primiparas reaches 50%, and for weakly expressed symptoms of MVP is about 12%.

In women older than 30 years, WLA occurs two times more often than in women at the age of 20–25. WLA leads to a prolonged course or complete stopping of labor, the appearance of signs of distress syndrome of the fetus, which causes operative delivery. In the structure of an emergency cesarean section, the WLA occupies the second to third place, reaching 37%.

The investigation of the causes of WLA concerns mainly the issue of the state of the myometrium without sufficient attention to the general anamnestic and clinical signs inherent in the MVP, although the causative factors of the WLA may indicate the possible involvement of MVP in the pathogenesis of an abnormality of labor [16].

The study of the features of the course of pregnancy and childbirth of women with small and large signs of MVP and CTD made it possible to establish that anomalies of labor in the first stage of childbirth appeared in 85.2% of women giving birth, compared to 33.9% in the control group without CDT. Cesarean section in the main group was performed in 12% of pregnant women and only in 4% of patients in the control group. Hypotonic bleeding in the III stage of labor took place in 7.3% of mothers with MVP and CTD and were absent in the control group. The discrepancy of the pubic joint was diagnosed in 7.2% of women with MVP and CTD and was not detected in the control group.

The birth traumatism of newborns from mothers with MVP and CTD was diagnosed in 34.4% of cases compared with 3.4% in the control group. This study showed that patients with generalized manifestations (involvement of three or more organs in the connective tissue defect) of MVP and CTD even in the absence of severe forms of this pathology constitute a high-risk group for the formation of obstetric and neonatal pathology.

The frequent occurrence of MVP and CDT in pediatric practice, the pronounced clinical polymorphism, and multiple organ changes make the problem relevant from the point of view of differential diagnostics and complex therapy.

Hemodynamic changes that develop during pregnancy, during childbirth, and in the postpartum period (primarily changes in bcc and cardiac ejection) cannot but affect the current of the woman's cardiovascular diseases. As well as diseases of the heart and blood vessels can adversely affect the course of pregnancy. Changes in hemodynamics in the mother have a negative effect on uteroplacental blood circulation, which in some cases may lead to the development of placental insufficiency, fetal growth retardation (FGR), and premature birth [4, 7, 16]. The central hemodynamics in women with mitral valve prolapse in the III trimester is characterized by an increase in the overall peripheral resistance of the vessels against a background of a decrease in volume indices, which indicates the voltage of the compensatory-adaptive mechanisms of the cardiovascular system [33].

The features of hemodynamics (heart rate, peripheral resistance of blood vessels, changes in blood pressure) are due to changes in the activity of the sympathoadrenal system. The pregnant women with MVP showed a significant decrease in MI and BV, as well as CI and BI as compared to those in women without MVP with a physiological pregnancy. Perhaps, the reduction of these indicators is due to a decrease in the contractility of the myocardium and a decrease in the activity of the sympathoadrenal system. Formation in the first trimester of

the hypokinetic type of central maternal hemodynamics with a reduced peripheral vascular resistance is one of the leading pathogenetic mechanisms of the development of preeclampsia and placental insufficiency (fetal hypoxia and IUGR) [4, 33].

The main clinical manifestation of placental insufficiency in patients with MVP is chronic intrauterine fetal hypoxia (7.33), which is detected in 34.5% of pregnant women, which is significantly higher than in women without MVP (13.2%). Dopplerometric examination of blood flow velocities revealed a violation of both placental and uterine-placental blood flow. In 11.2% of pregnant women with MVP on the background of chronic intrauterine fetal hypoxia, the fetal growth retardation (FGR) syndrome was detected, and in 84.4%—on the background of preeclampsia. In the development of placental insufficiency, the main and often initial causes are hemodynamic microcirculatory disorders. The factors that are genetically determined, exist in the maternal organism initially, also play a role in the formation of placental insufficiency, while the process of collagen formation has a certain role [7].

In the presence of a syndrome of non-differentiated dysplasia of connective tissue, the mother has the prerequisites for the birth of children with small developmental anomalies and congenital heart defects (MVP, TVP, left ventricular abnormal chords, patent foramen ovale, open arterial duct, atrial and interventricular septal defect). In children born from mothers with MVP, minor heart anomalies were detected in 16.4% [49].

The more significant clinical manifestations and a higher incidence of obstetric and perinatal complications are noted when MVP is combined with other intracardiac anomalies. Thus, in pregnant women with mitral valve prolapse and in combination with abnormally located chord and congenital heart disease (atrial septal defect), there is a significant increase in cardiac clinical symptoms from the first to the third trimester of pregnancy [5].

The postpartum period is characterized by a significant "positive" dynamics of ultrasound indicators of the degree of prolapse of the mitral valve and the degree of mitral regurgitation: they decrease reliably, even in comparison with the data during echocardiography in the first trimester of pregnancy. Thus, according to literature data [3, 5, 7, 10, 16, 41, 49, 50], women with MVP and other connective tissue anomalies of heart development are considered to be at high risk for complications of pregnancy, childbirth, and perinatal morbidity.

8. Conclusion

In connection with this, the following measures should be taken:

1. systematic prenatal supervision by an obstetrician and a cardiologist as during pregnancy, and at the stage of pregravid preparation;

2. in every trimester of pregnancy, it is necessary to carry out echocardiography, ECG, daily ECG monitoring;

3. investigation of the magnesium content in biological fluids and the detection of its deficiency in the appointment of magnesium preparations;

4. in case of complications of pregnancy and (or) complaints from the cardiovascular system—hospitalization;

5. systematic control of the fetus with the use of Doppler, cardiotocography, ultrasound in the detection of abnormalities timely correction;

6. labor is preferred to lead through the natural birth canal with adequate analgesia, under cardiac monitoring of the fetus and contractive activity of the uterus, prevention of abnormalities of labor. Cesarean section—according to obstetric indications;

7. examination of newborns with the help of echocardiography and consultation with a cardiologist and neurologist;

8. control echocardiography of a woman to determine the degree of prolapse of the mitral valve after delivery [33].

However, this algorithm is the opinion of only domestic obstetricians. According to data of some authors [3, 10], the complicated course of pregnancy and the increase in clinical symptoms in women with MVP are extremely rare. Women are primarily advised to avoid stressful situations, drinking coffee, strong tea, alcohol and tobacco, and using β-mimetics. Therapy is required only in the presence of arrhythmia (often tachycardia and extrasystoles). In this case, β-blockers are the drugs of choice. An interesting one is the recommendation of antibiotic prophylaxis in the presence of MVP and delivery with cesarean section in order to avoid infective endocarditis, but it is also controversial. The risk of serious complications in women with uncomplicated MVP younger than 45 years old is 0.2% per year.

Thus, the data presented earlier indicate a number of conflicting views on the etiology, classification, pathogenetic features of the mitral valve prolapsed, and the significance of its presence in the formation of various obstetric and perinatal complications. At present, it is urgent to continue research into the complex effects of nondifferentiated connective tissue dysplasia (NCTD) and MVP on the course of pregnancy, postpartum and neonatal delivery, analysis of current classifications of NCTD and pathogenetic (including genetic factors) of MVP features, and the definition of their importance in the development of obstetric complications.

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