

Thoracic aortic aneurysm in pregnancy: morphological analysis of 6 cases

V. P. Zakharova^{ID 1,3,A,C,D}, S. O. Siromakha^{ID *1,3,A,B,C,D}, Jolien W. Roos-Hesselink^{ID 4,D,E},
V. I. Kravchenko^{ID 1,B}, Yu. V. Davydova^{ID 1,2,B,F}, V. V. Lazoryshynets^{ID 1,E,F}

¹National M. Amosov Institute of Cardiovascular Surgery Affiliated to National Academy of Medical Sciences of Ukraine, Kyiv, ²SI "Institute of Pediatrics, Obstetrics and Gynecology named after Academician O. M. Lukyanova of National Academy of Medical Sciences of Ukraine", Kyiv, ³Bogomolets National Medical University, Kyiv, Ukraine, ⁴Erasmus University, Rotterdam, Netherlands

A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation; D – writing the article; E – critical revision of the article; F – final approval of the article

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*E-mail:

newsersir@gmail.com

Aortic dissection is rare but life-threatening complication in pregnancy, causing significant maternal and perinatal losses. Pregnancy may influence the integrity of the vessel wall and is a risk factor for dissection. There are very few data in the literature on structural changes in the aortic walls during pregnancy complicated by aortic dissection.

Aim. Study of pathological features in the wall of ascending aorta (AA) during or immediately after pregnancy is presented in the article.

Materials and methods. Material after surgical correction of AA in patients during pregnancy and in the early postpartum period was studied. Frozen sections were made from one part of the sample, followed by hematoxylin and eosin (H&E) staining, as well as Sudan III–IV staining to detect lipids. Paraffin sections were stained with H&E and picrofuchsin (van Gieson's stain) for differentiation of collagen and muscle fibers, as well as fuchselin (Weigert's elastic stain).

Results. Six cases of aortic surgery during pregnancy (n = 1) and postpartum period (n = 5) were included: severe aortopathy caused by Marfan syndrome (MS) (n = 3), aortic coarctation with bicuspid aortic valve (n = 1), renal hypertension (n = 1), and pregnancy-induced hypertension (n = 1). Pathohistological studies showed that in all patients who underwent aortic surgery at the end of the third trimester in the early postpartum period changes in aortic wall collagen structure were observed. In contrast, in a pregnant woman with MS and severe aortopathy, who underwent preventive aortic surgery at 19 weeks of gestation, there were no such changes, the morphologic samples showed areas of scarring. In all 6 cases signs of lipoidosis in the AA wall were observed.

All these data require further theoretical study, but clinicians are already faced with the question of the feasibility of preventive surgery in women with severe aortopathy on the preconception stage or during pregnancy.

Conclusions. The specific effect of pregnancy on the AA wall leads to collagen disruption and the appearance of lipoidosis in late pregnancy, which is an important pathomorphological substrate for the occurrence of acute aortic pathology.

Ключові слова:

аневризма аорти, розшаровуюча аневризма аорти, вагітність, синдром Марфана, морфологія аортальної стінки.

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Аневризма грудної аорти під час вагітності: морфологічний аналіз 6 випадків

В. П. Захарова, С. О. Сіромаха, Джолієн В. Роос-Геселінк,
В. І. Кравченко, Ю. В. Давидова, В. В. Лазоришинець

Розшарування аневризми аорти – рідкісне, але небезпечне для життя ускладнення вагітності, що призводить до чималих материнських і перинатальних утрат. У фаховій літературі обмаль даних про структурні зміни аортальних стінок під час вагітності, що ускладнена розшаруванням аорти.

Мета роботи – вивчення патогістологічних особливостей стінки висхідної аорти (ВА) під час або безпосередньо після вагітності.

Матеріали та методи. Дослідили матеріал після хірургічної корекції ВА в пацієнок під час вагітності та в ранньому післяпологовому періоді. З однієї частини зразка робили заморожені зрізи, забарвлювали гематоксиліном та еозином (H&E), а також суданом III–IV для виявлення ліпідів. Парафінові зрізи забарвлювали H&E та пікрофуксином (забарвлення за ван Гізоном) для диференціації колагенових і м'язових волокон, а також фукселіном (забарвлення за Вейгертом).

Результати. У дослідження залучили шість пацієнок, яким виконали операцію на аорті під час вагітності (n = 1) або в ранньому післяпологовому періоді (n = 5): із важкою аортопатією, спричиною синдромом Марфана (СМ) (n = 3), коарктацією аорти та двостулковим аортальним клапаном (n = 1), нирковою гіпертензією (n = 1), гіпертензією, що зумовлена вагітністю (n = 1). Патогістологічні дослідження показали: в усіх пацієнок, яких прооперували наприкінці III триместру гестації, в перші дні після розродження у стінках аорти реєстрували зміни колагену – набрякання та зниження тинкторіальних властивостей. У вагітної, яку прооперували превентивно на 19 тижні гестації, незважаючи на аортопатію, що спричинена СМ, такі зміни колагену не зафіксували; навпаки, у препаратах аорти цієї жінки були ділянки рубцевих змін. У всіх 6 пацієнок у стінках ВА спостерігали ознаки ліпоїдозу. Наведені відомості потребують продовження теоретичного вивчення, але перед клініцистами вже зараз стоїть питання про доцільність превентивних операцій у пацієнок із тяжкими аортопатіями на етапі прекоцепції або під час вагітності.

Висновки. Специфічний вплив вагітності на стінку ВА призводить до набрякання колагену та появи ліпоїдозу на пізніх термінах вагітності, що є важливим патоморфологічним субстратом для виникнення гострої патології аорти.

Аневризма грудной аорты при беременности: морфологический анализ 6 случаев

В. П. Захарова, С. О. Сиромеха, Джолиен В. Роос-Хесселинк,
В. И. Кравченко, Ю. В. Давыдова, В. В. Лазоришинец

Расслоение аневризмы аорты – редкое, но опасное для жизни осложнение беременности, приводящее к значительным материнским и перинатальным потерям. В научной литературе очень мало данных о структурных изменениях аортальных стенок при беременности, осложнённой расслоением аорты.

Цель работы – изучение патогистологических особенностей стенки восходящей аорты (ВА) во время или непосредственно после беременности.

Материалы и методы. Исследовали материал после хирургической коррекции ВА у пациенток во время беременности и раннем послеродовом периоде. Из одной части образца делали замороженные срезы, окрашивали гематоксилином и эозином (Н&Е), а также суданом III–IV для выявления липидов. Парафиновые срезы окрашивали Н&Е и пикрофуксином (окраска по ван Гизону) для дифференциации коллагеновых и мышечных волокон, а также фукселином (окраска эластических волокон по Вейгерту).

Результаты. В исследование включили шесть пациенток, перенёвших операцию на аорте во время беременности ($n = 1$) или в раннем послеродовом периоде ($n = 5$): с тяжёлой аортопатией, вызванной синдромом Марфана (СМ) ($n = 3$), коарктацией аорты и двустворчатым аортальным клапаном ($n = 1$), почечной гипертензией ($n = 1$), гипертензией, вызванной беременностью ($n = 1$). Патогистологические исследования показали: у всех пациенток, прооперированных в конце III триместра гестации, в первые дни после родоразрешения в стенках аорты фиксировали изменения коллагена – набухание и снижение тинкториальных свойств. У беременной, прооперированной превентивно на 19 неделе гестации, несмотря на аортопатию, обусловленную СМ, такие изменения коллагена не зафиксированы; напротив, в препаратах аорты этой пациентки отмечены участки рубцовых изменений. У всех 6 пациенток в стенках ВА отмечены признаки липоидоза. Эти данные требуют дальнейшего теоретического изучения, однако перед клиницистами уже сейчас стоит вопрос о целесообразности превентивных операций у пациенток с тяжёлыми аортопатиями на этапе прекоцепции или во время беременности.

Выводы. Специфическое влияние беременности на стенку ВА приводит к набуханию коллагена и появлению липоидоза на поздних сроках беременности, что является важным патоморфологическим субстратом для возникновения острой патологии аорты.

Ключевые слова:
аневризма аорты,
расслаивающая
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беременность,
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Pregnancy has a significant impact on the female body. In particular, the growth of the fetus, placenta and uterus requires increased functional activity of the maternal cardiovascular system [1,2]. The circulating blood volume increases by 30–40 %, heart rate and stroke volume increase, cardiac output increases by up to 30–50 % compared to non-pregnant women. Increase in cardiac preload is accompanied by an increase in size and weight of the woman [2].

Slightly decreasing blood pressure in the normal start of pregnancy is caused by a systemic decrease in vascular resistance [3], due to both neuro-mediated vasodilation and increased extensibility of the vascular wall [2,4]. The latter is associated with hormonal changes, in particular with a significant increase in estrogen and progesterone levels. The most important contributor responsible for dilatation of the arteries is probably relaxin, a hormone produced by the placenta. Experiments have shown that the activity of matrix metalloproteinase (MMP)-9 and MMP-2 increases in isolated small vessels in rats treated with relaxin. Also, in the aorta of rats during pregnancy, an increase in the expression of MMPs, in particular MMP-2 and MMP-3 [5], is described.

It has been suggested that weakening of the connective tissue matrix of the aortic wall by lysing enzymes promotes adaptation of this vessel to facilitate the increase in cardiac output. In normal pregnancy, the diameter of the ascending aorta (AA) increases by 1 mm [1]. In addition to the dilation of the AA, the increase in cardiac output associated with accelerated blood flow relative to the vascular wall may cause endothelium damage which can also contribute to the formation of

aortic aneurysms and even aortic dissection (AD) [6]. In women with heritable thoracic aortic disease, the risk of developing AD during pregnancy appears to be elevated, reaching a peak in the third trimester and the postpartum period [7].

Although AD is rare during pregnancy, its incidence during pregnancy is 14.5 vs. 1.24 per million in non-pregnant women [8]. It is an important clinical problem because it is associated with significant maternal (up to 17 %) and fetal (up to 42 %) mortality [9]. Information on aortic wall morphology will provide insight into the importance of pregnancy as a risk factor for AD, but only a few outdated case reports are currently available in the literature.

Aim

Therefore, the aim of the current study is to discuss pathohistological findings of aortic wall material in women who needed surgery due to AD or aneurysm during or immediately after pregnancy.

Materials and methods

This was a retrospective descriptive study in which we included female patients from cardiac surgical facility who underwent AA surgery during or immediately after pregnancy in the period between 2014 and 2020 and had histomorphological evaluation of the aortic wall.

Adult patients (≥ 18 years old) who presented with aortic surgery during pregnancy or in the postpartum period between 01/01/2014 and 01/01/2020 were included.

Table 1. Clinical data for the 6 patients who underwent AA surgery during pregnancy or immediately after delivery

Patient	Age	History	Diameter (mm) and primary aortic pathology	Complications during pregnancy (type, term)	Delivery (type, term, birth weight)	Gestation age (weeks) at the time of surgery	Type of surgical procedure
A	22	MFS (z-score 12.8, ectopia lentis) Primigravida	AA 45 mm Valsalva sinus 62 mm		C-section 38 weeks 2440 g	19 weeks	BP with pregnancy preservation
B	24	MFS (z-score 3.2 FBN1) Primigravida	AA 42 mm Valsalva Sinus 42 mm	AAAD 40 weeks	C-section 40 weeks 3350 g	40 weeks, 26 hours after C-section	BP 5 days after BP rupture of the abdominal aorta, maternal mortality caused by bleeding
C	36	MFS (family history z-score 7.9, ectopia lentis) Primigravida	AA 45 mm Valsalva sinus 41 mm	AAAD 6 th day after C-section	C-section 35 weeks IVF Twins 2400 g, 2000 g	Day 6 after C-section	BP with hemiarch reconstruction
D	32	Renal hypertension 2003 AAAD 2013 TEVAR (CAAD) Primigravida	AA 59mm CAAD	AAAD 36 weeks	C-section 36 weeks 2690 g	23 hours after C-section	SAAR with hemiarch
E	28	C-section 4 years earlier	AA 43 mm BAV + CoA Hypertension	AAAD 4 th day after C-section	C-section 38 weeks 2800 g	Day 4 after C-section	Endovascular CoA repair then SAAR
F	38	Unremarkable Previous 1 successful pregnancy	AA 46 mm	AAAD 38 weeks preeclampsia	C-section 38 weeks 3300 g	28 hours after C-section	BP with hemiarch reconstruction (valve conduit)

AA: ascending aorta; **C-section:** caesarean section; **BP:** Bentall procedure; **AAAD:** acute ascending aortic dissection; **TEVAR:** transthoracic endovascular aortic reconstruction; **CAAD:** chronic ascending aortic dissection; **SAAR:** supracoronary ascending aortic replacement; **BAV:** bicuspid aortic valve; **CoA:** aortic coarctation; **IVF:** in vitro fertilization.

Patients were identified through searches in the local cardiothoracic surgery database. Data were collected from the hospital digital patient files and internal institutional database.

Patients with thoracic aortic aneurysm or AD are treated according to the European guidelines on aortic disease (ref: ESC aorta). In pregnant patients, the timing for aortic surgery is based on the indication and whether the fetus is viable or not (ref: ESC guidelines pregnancy). In case of an AA aneurysm with indication for surgery and gestation age of <24 weeks, the operation is performed with the fetus in situ. When the fetus is viable, the aortic surgery is performed after caesarean section. In case of acute AA dissection, emergency operation is performed.

Fragments of the aortic wall excised during the operation were fixed in 10% neutral formalin. Frozen sections were made from one part of the sample, followed by hematoxylin and eosin (H&E) staining, as well as Sudan III–IV staining to detect lipids. The remaining material in the form of 1–2 pieces was dehydrated in alcohol of increasing concentration and enclosed in paraffin. Paraffin sections were stained with H&E and picrofuchsin (van Gieson's stain) for differentiation of collagen and muscle fibers, as well as fuchselin (Weigert's elastic stain).

Results

The study population consisted of 6 women (mean age 30.0 ± 6.5 years), 3 of them had Marfan syndrome (MFS). Baseline characteristics are shown in *Table 1*.

Of the three women with MFS, in one (patient B) the diagnosis was confirmed by genetic research and in the other two it was highly suspected based on family history and the presence of ectopia lentis.

Due to the high risk of AD or even rupture (AA diameter 45 mm and aortic sinuses 62 mm), patient A agreed to have preventive surgery, and she underwent Bentall procedure at 19 weeks of gestation. At 38 weeks, she

gave birth to a healthy baby by elective C-section. Histological examination of the operative material in the wall of her aorta revealed signs of elastopathy: elastic membranes (EM) were heterochromic (mostly pale), thinned, fragmented and disorganized. In many fields of view, there were areas almost completely devoid of fuchselinophilic structures (*Fig. 1A*). Defects of the elastic framework of the aortic wall were replaced by collagen: more mature in the deeper layers of the media and loose, swollen in the subintimal layer (*Fig. 1B*). Against this background, individual clusters of smooth muscle cells (SMCs) were differentiated, which, being enclosed in fibrous tissue, retained a predominantly circular orientation (*Fig. 1B, C*). The intima was thickened due to fibromuscular proliferation and edema, and microfractures were visualized on its surface (*Fig 1A, B*). Microgranular lipids were detected in the intima during Sudan III–IV staining.

Patient B, 24 years old, had known MFS (genetically confirmed), had favorable course of all trimesters of pregnancy, but at 40 weeks she developed AAAD. She underwent an emergency C-section and 26 hours later a Bentall procedure. Both operations were successful, the child remained alive and well. However, 5 days after cardiac surgery, the patient had a rupture of the abdominal aorta with massive bleeding and fatal outcome. Histological changes in the wall of the AA were largely the same as in the previous case. However, the areas devoid of elasticity were wider (*Fig. 2A*), and the collagen fibers were “blurred”, multidirectional, scattered, and pale when stained with van Gieson's picrofuchsin (*Fig. 2B*). As a result, whole layers of smooth muscle cells (SMCs), devoid of the elasto-collagen matrix, were directed fan-shaped, from the deep layers of the media towards the intima (*Fig. 2C*). The latter showed signs of surface destruction (*Fig. 2B*), dissection (*Fig. 2A*) and lipid infiltration (*Fig. 2D*).

Patient C was 36 years old and also had known MFS. Her pregnancy went smoothly and at 40 weeks she underwent C-section. However, on the 6th day after

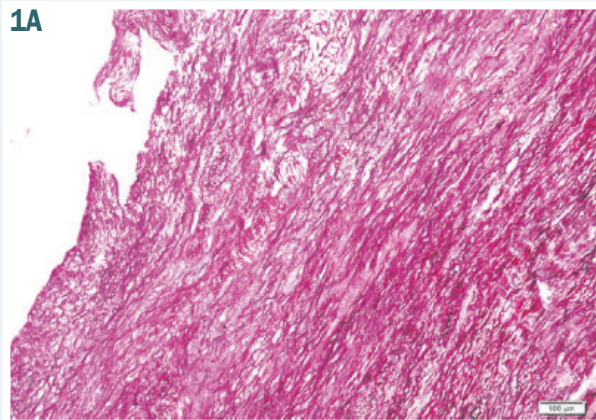


Fig. 1. Patient A, MFS. AA wall fragment. **A.** Defect of the elastic framework of the media; fuchselin staining, $\times 100$. **B.** Replacement fibrosis; picrofuchsin staining, $\times 200$. **C.** Intimal tear; H&E staining, $\times 40$.

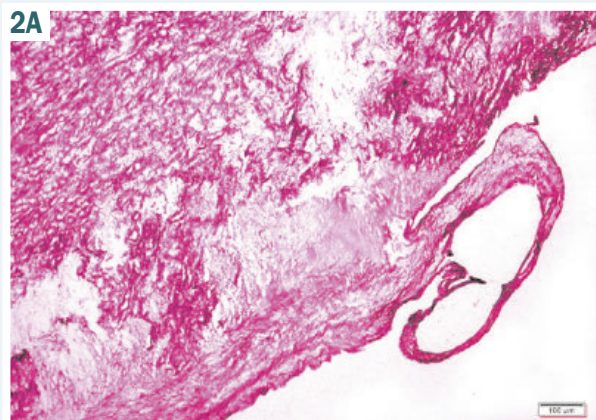
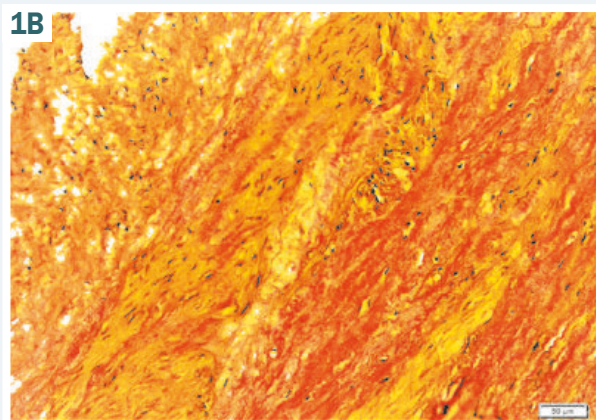
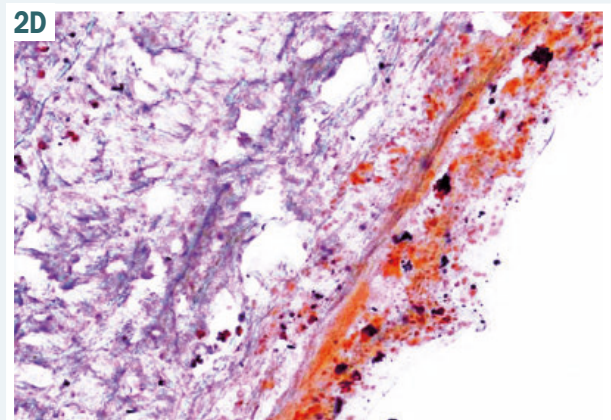
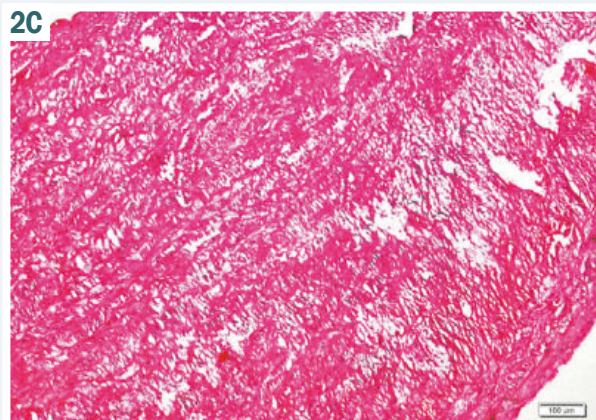
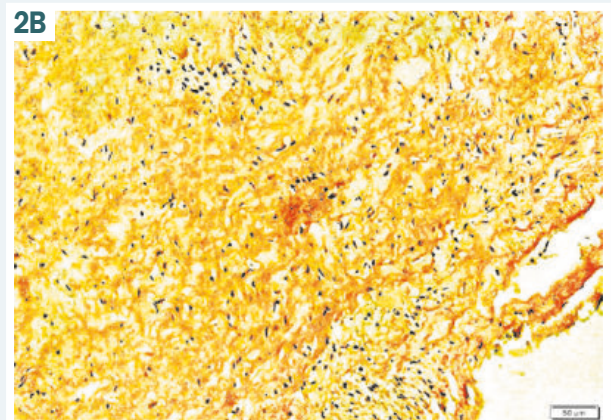
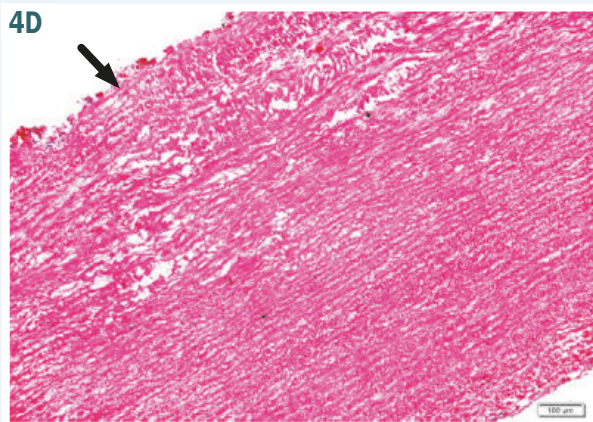
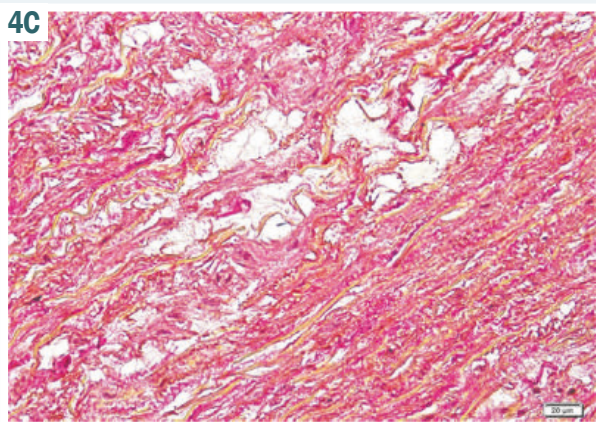
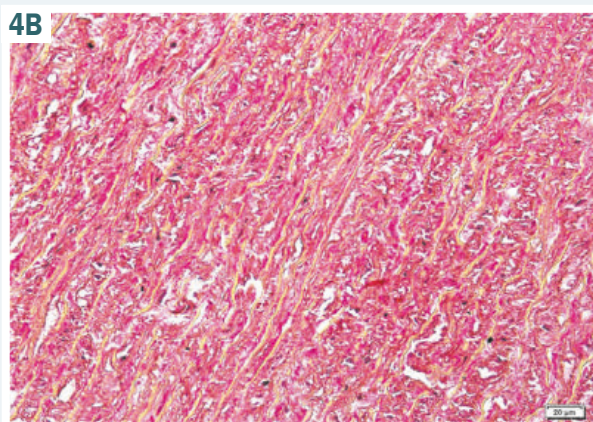
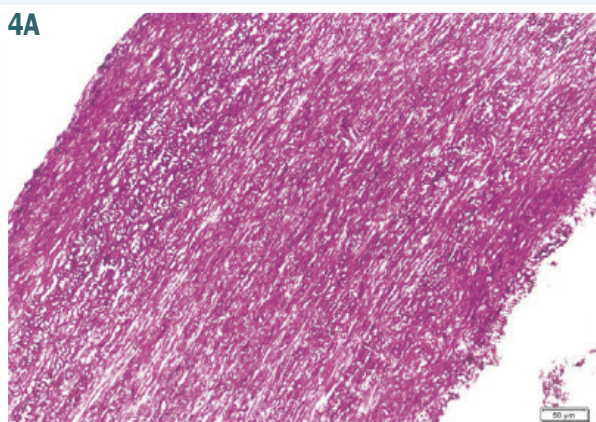
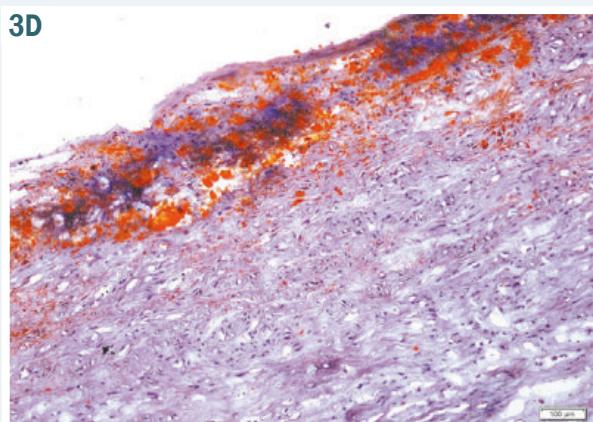
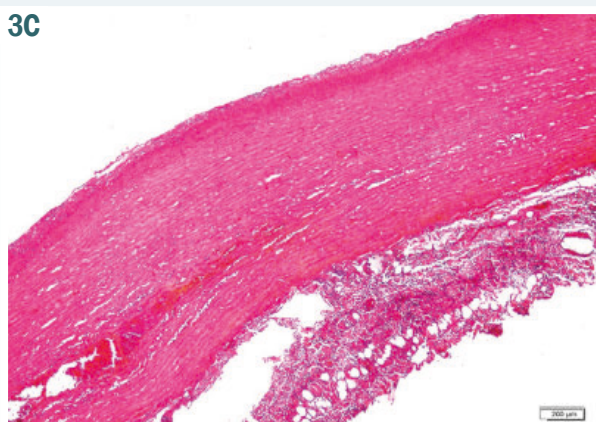
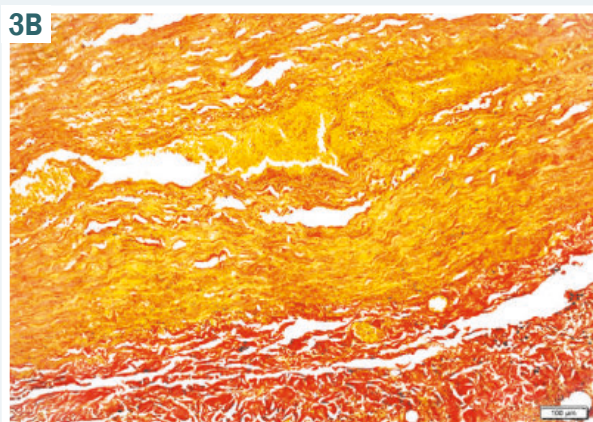
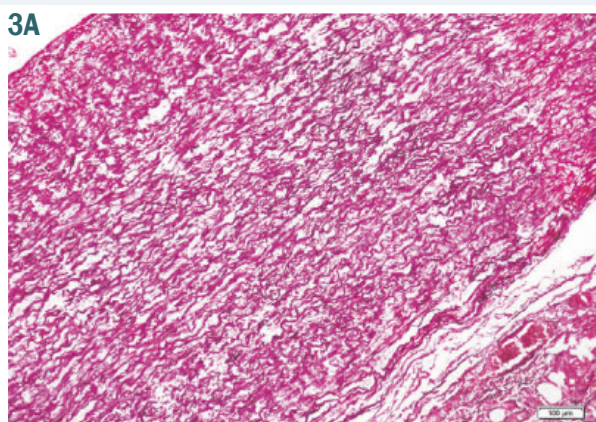


Fig. 2. Patient B, MFS. AA wall fragment. **A.** Elastopathy of the media with the destruction of elastic membranes, rupture of the intima; fuchselin staining, $\times 100$. **B.** Collagen is thinned, pale, disorganized; picrofuchsin staining, $\times 100$. **C.** Disorientation, dystrophy, necrosis of SMCs; H&E staining, $\times 100$. **D.** Intima lipid deposition; Sudan III–IV staining, $\times 200$.





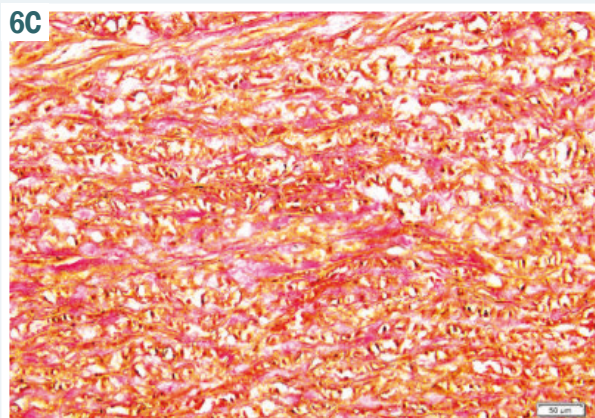
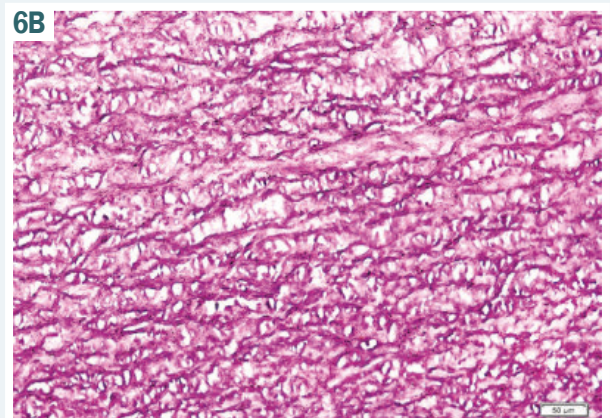
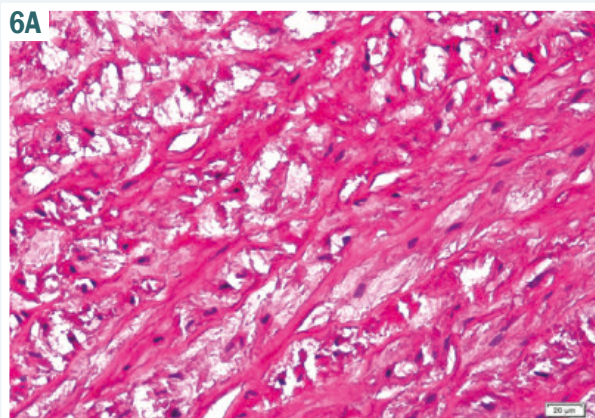
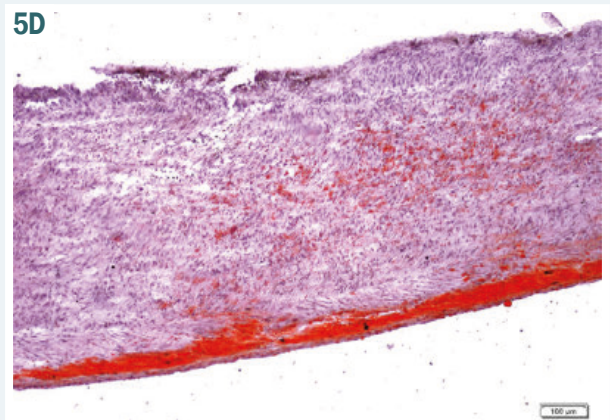
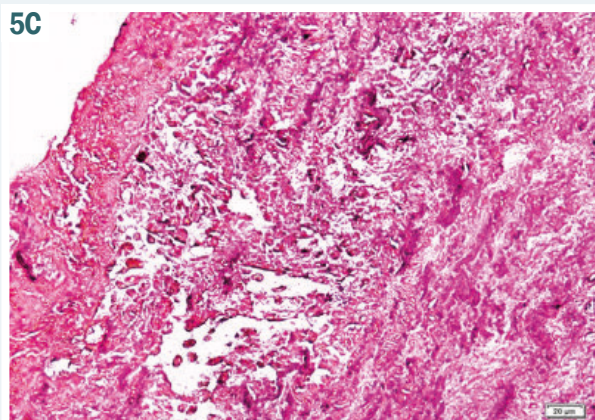
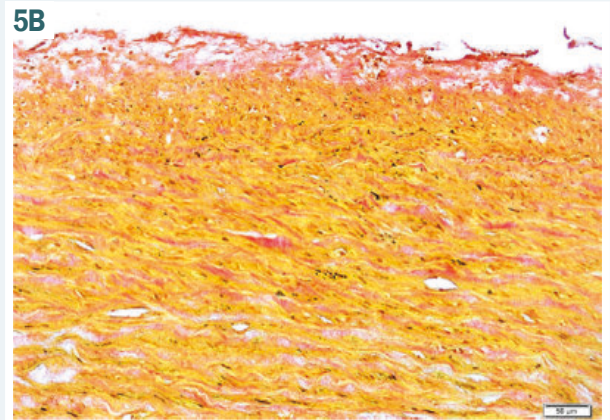
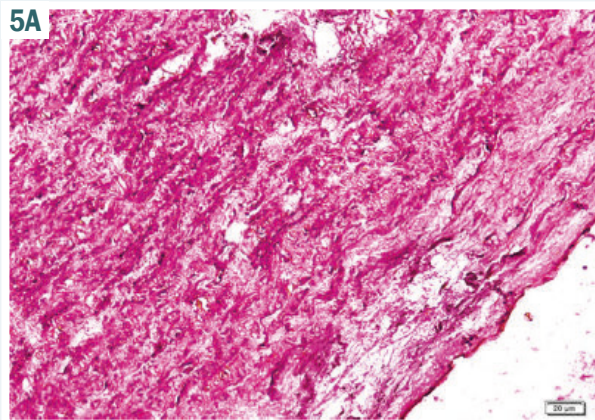


Fig. 3. Patient C, MFS, AA wall fragment. **A.** Defibering and polymorphism of EM of the media; fuchselin staining, $\times 100$. **B.** Swelling of the collagen fibers of the media; picrofuchsin staining, $\times 100$. **C.** Leukocyte infiltration of the adventitia, media dissection; H&E staining, $\times 40$. **D.** Lipoidosis of the intima and subintimal layer of the media; sudan III-IV staining, $\times 100$.

Fig. 4. Patient D, renal hypertension, AA wall fragment. **A.** The EM of the media are stretched, collapsed in the middle layer; fuchselin staining, $\times 100$. **B.** The intercellular matrix of the media is represented mainly by collagen; picrofuchsin staining, $\times 400$. **C.** Collagen lysis with the destruction of other media structures; picrofuchsin staining, $\times 400$. **D.** The plane of stratification of the aortic wall (arrow) in the area of its destruction; H&E staining, $\times 100$.

Fig. 5. Patient E, CoA, BAV, AA wall fragment. **A.** Chains of fuchselinophilic granules are observed on the sides of individual fragments of elastic membranes; fuchselin staining, $\times 400$. **B.** Collagen of the extracellular matrix is hypochromic, swollen; picrofuchsin staining, $\times 200$. **C.** Dissection of the AA wall in the area of lysis of collagen and other structures; fuchselin staining, $\times 400$. **D.** Intimal and media lipoidosis in the area of smooth muscle cell destruction; Sudan III-IV staining, $\times 100$.

Fig. 6. Patient F, Preeclampsia, 38 weeks of gestation, AA wall fragment. **A.** Intra- and extracellular edema; H&E staining, $\times 400$. **B.** Dissociation and ruptures of elastic membranes; fuchselin staining, $\times 200$. **C.** Swelling and lysis of collagen; picrofuchsin staining, $\times 200$.

delivery, she developed AAAD. On the same day, she underwent a Bentall procedure including reconstruction of the hemiarch. Judging by the sample of the aortic wall excised during the operation, its microstructure, in this case, differed from the first two observations. No areas devoid of EM were found in histological preparations. However, all available membranes differed in polymorphism due to their defibering with different thickness, length, and degree of corrugation of each fiber, which also differed in tinctorial properties (Fig. 3A). Such features of the elastic framework of AA definitely reduced its ability to model the diameter of the vessel in accordance with the systolic-diastolic fluctuations of blood pressure on its wall. In addition, patient C, as well as B, had changes in the collagen fibers of the media, which (in contrast to adventitia) were pale intermittent and without clear contours (Fig. 3B). This reduced the mechanical strength of AA. This patient also had signs of nonspecific inflammation in the adventitia (Fig. 3C) and significant lipoidosis of the intima and subintimal layers of the media (Fig. 3D).

Patient D, 32 years old, suffered from renal hypertension for many years. In 2003, she developed AAD type B according to the Stanford classification without serious hemodynamic consequences. The patient was treated conservatively, maintaining optimal blood pressure. In 2013, she underwent endovascular reconstruction of the thoracic aorta (TEVAR) due to its chronic dissection and dilation up to 59 mm. In 2019, she became pregnant. At 36 weeks of gestation, AAAD occurred, which extension to the left side of the aortic arch. An emergency C-section was performed (the child survived), and 48 hours later supracoarctary ascending aortic replacement (SAAR) with a hemiarch was performed.

At microscopy in all samples the effect of overstretching and convergence of fibrous structures of media was found, especially expressed in its middle layer (Fig. 4A). EM in this area were straightened, pale, discontinuous, and as if fused into conglomerates due to the growth of collagen (Fig. 4B) which was predominant component of the AA wall. The number of SMCs was reduced, the nuclei of most of them had an elongated shape. Signs of collagen lysis with the destruction of EM and SMCs were observed in the subintimal and outer layers of the media (Fig. 4C) and later – at the zone of dissection (Fig. 4D). In the aortic intima of patient D, focal accumulations of lipophages and lipid granules were noted.

Patient E, 28 years old, was diagnosed with congenital pathology of the aorta: isthmus coarctation as well as a bicuspid aortic valve (BAV). Four years earlier the patient gave birth to a child by C-section on obstetric indications. The current pregnancy ended at 38 week also by elective C-section. But on the 4th day after delivery, the mother was diagnosed with AAAD. She underwent emergency CoA stenting and then, at the same day, SAAR. Both the mother and the child were discharged in satisfactory condition after 11 days.

Such aspects of the pathogenesis of AA lesion as increased transmural pressure on the wall of AA and the aortic arch in the precoarctation basin and eccentric traumatic for aortic wall transannular blood flow were considered in the histopathological study of preparations from the internal layer of the dissected aortic wall

of the patient E. The expected straightening of the EM of the media was noticeable, but only in some areas of the subintimal layer. On the rest of the sample, the media was virtually devoid of an integral elastic framework as a result of thinning, lysis and fine fragmentation of EM (Fig. 5A). On both sides of the largest fragments of EM, small fuchselinophilic granules are observed (Fig. 5A), which have been described in patients with a certain variant of the elastin gene polymorphism [11]. The spaces between the components of the elastic structures of the aortic wall are filled with collagen, but its fibers were hypochromic, swollen (Fig. 5B), and lysed together with SMCs and EM in the area of dissection (Fig. 5C), with early manifestations of perifocal inflammation. Also, in the samples of patient E, there was a positive reaction to lipids in the intima and the area of dystrophy and necrobiosis of media SMCs (Fig. 5D).

Patient F has had no history of pre-pregnancy risk factors, for aortic disease. However, at 38 weeks of gestation, she previously developed preeclampsia and then – AAAD. In this regard, the patient underwent C-section, and 28 hours later Bentall procedure with the reconstruction of the arch with a valve-containing conduit. The mother and the child survived and were discharged home in satisfactory condition. The samples of the aortic wall revealed signs of pronounced intracellular edema of the SMCs (Fig. 6A), accompanied by edema of the extracellular matrix with increase in the distance between the EM and destruction of some of them (Fig. 6B). In collagen fibers, swelling and edema were accompanied by lysis (Fig. 6C). In this case, as well as in 4 other patients, lipophages and lipid granules were also found in the intima with damaged endothelium.

Discussion

In this paper we described 6 women with aortic surgery during pregnancy or in the postpartum period with detailed morphological description. In 4 cases the pregnancy occurred against the background of initial aortic pathology and one woman suffered from known hypertension. The sixth case, however, had no premorbid risk factors. She developed an acute increasing of blood pressure (preeclampsia) during pregnancy, which is the only factor that could contribute to the occurrence of the acute dissection. In this series maternal mortality was 17 % (n = 1), however, we avoided perinatal losses, probably because we were able to perform C-section before aortic surgery was done in 5 of the 6 women. Timely diagnosis of aortic pathology and counselling of women wishing to become pregnant may prevent the occurrence of life-threatening complications during pregnancy.

In patient A aortic surgery was performed during the second trimester of pregnancy. The morphological changes, which were found in the aortic wall of this patient, testified to the extremely high risk of dissection or rupture, so the preventive surgical treatment should be considered as a life-saving intervention. Two other patients with MFS did not escape of acute aortic dissection, one at the end of pregnancy and the other in the first week after delivery.

Acquired morphological lesions of the aortic wall in patient D were the cause of recurrent AAD at 36 weeks of gestation. Primary damage to the aortic wall and

the primary episode of AAD are most likely related to renal hypertension, which is one of the causes of overextension of the EM of the media with the subsequent remodeling of all structures.

It is known that one of the main manifestations of CoA is hypertension in the proximal to coarctation segment (AA, arch, and brachiocephalic branches), which is combined with hypotension of the descending aorta and its branches. That is, from birth AA and the arch function in conditions of increased transmural pressure, which with age leads to morphological changes in its structure in the form of stretching and thinning of EM and strengthening of the collagen component of the connective tissue matrix [11]. As a result, the AA wall loses elasticity and becomes more rigid which reduces its ability to distend and shrink in response to pulsatile flow and increases the traumatic effect of blood flow on the endothelium.

The state of AA (patient E), in addition to CoA could also be affected by BAV. Usually in this pathology, the aortic valve is located eccentrically. Due to this, the transvalvular blood flow can deviate from the longitudinal axis of the AA towards one of its walls, exerting a direct mechanical impact on it and creating additional traumatic intimate turbulent flows. The combination of BAV and CoA could associate with heritable thoracic aortic pathology as well [12]. Such pathomorphological mechanisms probably provoked the development of aortic aneurysm and later AAD in this patient.

Regardless of the nature of the occurrence, all the factors that contributed to AAAD caused either weakening of the mechanical strength of the structure of the aortic wall, or a significant increase in the load, or both. This is applicable for any case of aortic aneurysm formation and dissection/rupture of its walls. However, in pregnant women, due to the increase in circulating blood volume, there is a physiological decrease in vascular resistance [3,4], in particular, due to increased elasticity of the artery walls. Animal experiments have shown the role of placental-produced relaxin in the increased activity of MMPs which weaken the connective tissue matrix of blood vessels, including the aorta [5].

According to our data, in all patients operated at the end of gestation and in the early postpartum period, changes in collagen in the form of its swelling and decrease in tinctorial properties were observed in the aortic wall. In the pregnant woman with MFS who underwent surgical intervention preventively at 19 weeks of gestation, there were no such changes in collagen. On the contrary, the samples showed areas of scar replacement by collagen of EM and SMCs destroyed because of MFS. That is, we can assume that in the early stages of pregnancy, changes in the aortic wall that occurred before pregnancy are not exacerbated by physiological mechanisms of reducing vascular resistance. Also noteworthy is the fact that all 6 patients had signs of lipoidosis in the walls of the AA. This may be due to factors causing damage to the intima, such as the initial pathology of the aorta, trauma to the endothelium by blood flow, as well as possible changes in lipid metabolism.

This requires further theoretical study, but clinicians have already faced the question of indications for preventive surgery in pregnant women with different variants of

aortic pathology [6,10]. Indeed, from our study we now have some evidence that pregnancy has specific effects on the aortic wall and is associated with a higher risk of dissection, but of course we have to be careful to draw firm conclusions, because the numbers are small and the cases are highly selected on their need for aortic surgery. It will not be possible to study the aortic wall in pregnant patients without surgery. Perhaps future animal study can be of help here. Also, here further research is warranted.

Limitations

The number of patients in this study is limited and they are selected based on their need for surgery. Therefore, our data may not be considered representative for all pregnant women with and without aortic pathology. In the three patients with assumed MFS only one case was genetically proven and, therefore, the diagnosis in the other two is not definitive; however, there is a high suspicion based on their family history and eye abnormalities. The study of pathohistological features of the AA wall with detection of MMPs should be obligatory included. Useful information can be obtained from studies of relaxin in the blood of pregnant women.

Conclusions

1. Swelling and lysis of collagen on the background of initial aortic pathology are noted in the aortic wall of pregnant women. These features reduce the mechanical strength of the aortic wall. The described changes in collagen can be associated with specific hormonal and hemodynamic changes in the female body in late pregnancy.
2. In a patient who underwent preventive surgery at 19 weeks of gestation, such changes in collagen in AA were not detected, despite significant damage to its wall due to MFS, in the form of initial detachment of the intima.
3. Signs of early lipoidosis in AA preparations were detected in all 6 cases.
4. In women who underwent AA surgery during pregnancy or the postpartum period, clear changes were observed in the aortic wall, that can be attributed to the hormonal and hemodynamic impact of pregnancy in late pregnancy, with more advanced changes in collagen. This study supports the theory that pregnancy is a risk factor for aortic complications, especially in women with premorbid aortic pathology.

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Information about authors:

Zakharova V. P., MD, PhD, DSc, Professor, Head of the Department of Pathology with Pathological Anatomy, National M. Amosov Institute of Cardiovascular Surgery Affiliated to NAMS of Ukraine, Kyiv; Professor of the Department of Pathological Anatomy, Bogomolets National Medical University, Kyiv, Ukraine. ORCID ID: [0000-0001-5146-6845](https://orcid.org/0000-0001-5146-6845)

Siromakha S. O., MD, PhD, Chief Medical Officer, National M. Amosov Institute of Cardiovascular Surgery Affiliated to NAMS of Ukraine; Associate Professor of the Department of Surgery 2, Bogomolets National Medical University, Kyiv, Ukraine. ORCID ID: [0000-0002-7031-5732](https://orcid.org/0000-0002-7031-5732)

Jolien W. Roos-Hesselink, MD, PhD, Professor, Head of the Department of Adult Congenital Heart Disease, Erasmus University, Rotterdam, Netherlands. ORCID ID: [0000-0002-6770-3830](https://orcid.org/0000-0002-6770-3830)

Kravchenko V. I., MD, PhD, Head of the Department of Surgical Treatment of Aortic Pathology, National M. Amosov Institute of Cardiovascular Surgery Affiliated to NAMS of Ukraine, Kyiv. ORCID ID: [0000-0003-4873-5367](https://orcid.org/0000-0003-4873-5367)

Davydova Yu. V., MD, PhD, DSc, Professor, Head of the Department of Obstetric Problems of Extragenital Pathology, Institute of Pediatrics, Obstetrics and Gynecology named after Academician O. M. Lukyanova of NAMS of Ukraine; Chief Researcher of the Department of Congenital Heart Diseases in Children, National M. Amosov Institute of Cardiovascular Surgery Affiliated to NAMS of Ukraine, Kyiv. ORCID ID: [0000-0001-9747-4738](https://orcid.org/0000-0001-9747-4738)

Lazoryshynets V. V., MD, PhD, DSc, Professor, Academician of NAMS of Ukraine, Director of National M. Amosov Institute of Cardiovascular Surgery Affiliated to NAMS of Ukraine, Kyiv. ORCID ID: [0000-0002-1748-561X](https://orcid.org/0000-0002-1748-561X)

Відомості про авторів:

Захарова В. П., д-р мед. наук, зав. відділу патології з патологічною анатомією, ДУ «Національний інститут серцево-судинної хірургії імені М. М. Амосова НАМН України»; професор каф. патологічної анатомії, Національний медичний університет імені О. О. Богомольця, м. Київ, Україна.

Сіромаха С. О., канд. мед. наук, головний лікар, ДУ «Національний інститут серцево-судинної хірургії імені М. М. Амосова НАМН України»; доцент каф. хірургії № 2, Національний медичний університет імені О. О. Богомольця, м. Київ, Україна.

Джолієн В. Роос-Гесселінк, PhD, професор, зав. відділу вроджених вад серця у дорослих, Університет Еразмус, м. Роттердам, Нідерланди.

Кравченко В. І., канд. мед. наук, зав. відділу хірургічного лікування патології аорти, ДУ «Національний інститут серцево-судинної хірургії імені М. М. Амосова НАМН України», м. Київ. Давидова Ю. В., д-р мед. наук, професор, зав. відділення акушерських проблем екстрагенітальної патології, ДУ «Інститут педіатрії, акушерства і гінекології імені академіка О. М. Лук'янової НАМН України»; головний науковий співробітник відділення вроджених вад серця у дітей, ДУ «Національний інститут серцево-судинної хірургії імені М. М. Амосова НАМН України», м. Київ.

Лазорішинець В. В., д-р мед. наук, академік НАМН України, професор, директор ДУ «Національний інститут серцево-судинної хірургії імені М. М. Амосова НАМН України», м. Київ.

Сведения об авторах:

Захарова В. П., д-р мед. наук, зав. отделом патологии с патологической анатомией, ГУ «Национальный институт сердечно-сосудистой хирургии имени Н. М. Амосова НАМН Украины»; профессор каф. патологической анатомии, Национальный медицинский университет имени А. А. Богомольца, г. Киев, Украина.

Сиромакха С. О., канд. мед. наук, главный врач, ГУ «Национальный институт сердечно-сосудистой хирургии имени Н. М. Амосова НАМН Украины»; доцент каф. хирургии № 2, Национальный медицинский университет имени А. А. Богомольца, г. Киев, Украина.

Джолієн В. Роос-Гесселінк, PhD, професор, зав. відділом вроджених пороков серця у дорослих, Університет Еразмус, г. Роттердам, Нідерланди.

Кравченко В. И., канд. мед. наук, зав. отделом хирургического лечения патологии аорты, ГУ «Национальный институт сердечно-сосудистой хирургии имени Н. М. Амосова НАМН Украины», г. Киев.

Давидова Ю. В., д-р мед. наук, профессор, зав. отделением акушерских проблем экстрагенитальной патологии, ГУ «Институт педиатрии, акушерства и гинекологии имени академика Е. М. Лукьяновой НАМН Украины», главный научный сотрудник отделения врожденных пороков сердца у детей, ГУ «Национальный институт сердечно-сосудистой хирургии имени Н. М. Амосова НАМН Украины», г. Киев.

Лазорішинець В. В., д-р мед. наук, академік НАМН України, професор, директор ГУ «Національний інститут серцево-судинної хірургії імені Н. М. Амосова НАМН України», г. Київ.

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