https://doi.org/10.30702/ujcvs/22.30(04)/TG056-5965
UDC 616.132.1-007.21-053.2

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Restenosis Rate and Reinterventions after Aortic Arch Repair in Infants

Abstract

The aim. This study aims to determine the reintervention rate in infants undergoing aortic arch repair and to analyze risk factors and evaluate the results of reinterventions.

Materials and methods. This retrospective study examines 445 infants with aortic arch hypoplasia who underwent aortic arch reconstruction between 2011 and 2019. The study included only patients with two-ventricle physiology and subsequent two-ventricle repair. Techniques for primary repair included extended end-to-end anastomosis (n = 348), end-to-side anastomosis (n = 611), autologous pericardial patch repair (n = 16).

Results. The overall mortality in the entire study group was 3.3 %. Follow-up period ranged from 1 month to 9.4 years (mean 2.8 ± 2.5 years). Restenosis at the site of aortic arch repair was identified in 47 (10.5 %) patients. Of these, 12 patients underwent surgical reconstruction of the aortic arch, 27 patients underwent balloon angioplasty, and in 8 patients both methods were used. Freedom from reintervention was 89.4 % at 1-year follow-up and 87.5 % at 4-year follow-up. The most determining factors for restenosis were related to hypoplastic proximal aortic arch and body weight less than 2.5 kg.

Conclusions. Surgical treatment of aortic arch hypoplasia in newborns and infants is effective and shows good immediate and long-term results. Anatomical correction of reobstruction at the level of the aortic arch is safe with both endovacular and surgical methods with low mortality and incidence of repeated interventions. Identified risk factors for mortality and recurrent aortic arch interventions help to improve the treatment of aortic arch hypoplasia in patients under 1 year of age.

Keywords: *recurrent obstruction, balloon angioplasty, surgical reconstruction, risk factors for mortality, hypoplasia.*

Introduction. Aortic coarctation accounts for 5 **%** to 8 **%** of congenital heart diseases in children and is frequently associated with aortic arch hypoplasia [1]. Recurrent aortic arch obstruction remains an important complication after aortic arch reconstruction in infants and occurs in a number of patients in surgical series [2, 3]. In literature there are many studies on risk factors of reobstruction after aortic arch repair in infants. Despite many different techniques for arch reconstruction, some authors announced that the restenosis rate is directly associated with arch anatomy and the type of repair [4].

It is often thought that age at time of reconstruction, low weight in neonates, and preoperative care are associated with higher risk of recurrent obstruction [5].

The recurrence rate of arch obstruction and recurrent interventions varies in different series and ranges from 2 % to 40 % [6, 7]. There is currently no consensus on the optimal methods for recurrent aortic obstruction. Strategies to treat recurrent aortic arch obstruction have evolved with time [8, 9]. Over the last 2 decades, balloon angioplasty has been more widely used, but a number of publications still recommend surgery as a more effective treatment for re-

stenosis at the site of previous aortic arch repair. The aim of our study is to determine the reintervention rate in infants undergoing aortic arch repair and to analyze risk factors and evaluate the results of reinterventions.

Materials and methods. The study included 445 neonates who underwent aortic arch repair due to aortic coarctation with aortic arch hypoplasia at the National Amosov Institute of Cardiovascular Surgery of the NAMS of Ukraine and the Ukrainian Children's Cardiac Surgery Center from 2011 to 2019. The study included only patients with two-ventricle physiology and subsequent two-ventricle repair. Exclusion criteria: infants with single-ventricle physiology. Aortic coarctation with aortic arch hypoplasia occurred as an isolated defect in 159 (35.7 %) patients, and was associated with other cardiac malformations in 286 (64.3 %) patients. There were 284 (63.8 %) males and 161 (36.2 %) females. The mean age of the patients at first operation was 2.3 ± 0.8 months, mean weight was 4.8 ± 1.9 kg. Reinterventions on the aortic arch were performed in 47 (10.5 %) patients who formed the main group of the study. Primary aims included an analysis of restenosis rates and catheter-based or surgical reinterventions for aortic arch obstruction. Characteristics of the patients at the time of reintervention are listed in Table 1.

As we can see, the most common surgical technique used at primary aortic arch repair was extended end-to-end anastomosis through a lateral thoracotomy. All the patients underwent routine transthoracic echocardiography. Anatomical description of the aortic arch was analyzed from echocardiographic data. The diagnosis of aortic arch hypoplasia was established if the deviation of the isthmus distal and proximal aortic arch Z-score was less than or equal to -2. Aortic aneurysm formation was determined if the diameter of the aneurysm was 1.5 times greater than that of the descending aorta at the level of the diaphragm. Reinterventions after primary aortic arch repair included 27 (6.1 %) catheter-based reinterventions, 12 (2.7 %) surgeries, and in 8 patients (1.8 %) both techniques were used (Fig. 1).

Table 1

Patient characteristics at the time of reintervention

Characteristics	Reintervention group, n = 47
Age, month	5.8 ± 3.0
Weight, kg	5.9 ± 2.7
Body surface area, m^2	0.24 ± 0.04
Surgical techniques	
Extended end-to-end anastomosis	38 (80.9 %)
End-to-side anastomosis	8 (17 %)
Autologous pericardial patch aortoplasty	1 (2.1 %)
Surgical approach	
Thoracotomy	32 (68 %)
Median sternotomy	15 (32 %)

The most common indication for reintervention was recurrent aortic obstruction at the site of previous arch repair. However, 1 patient had restenosis at the proximal arch and aortic aneurysm at the distal arch after patch aortoplasty. Indications for reintervention after primary aortic arch repair were upper extremity/lower extremity resting

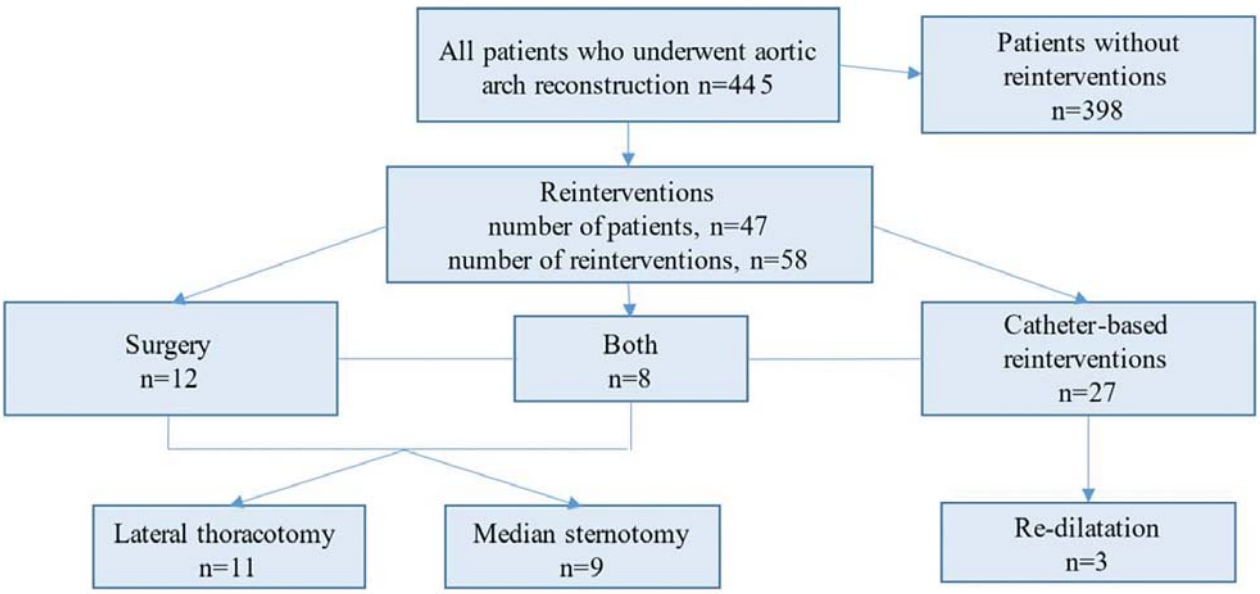

Fig. 1. *Aortic arch reinterventions (surgeries and endovascular interventions)*

peak-to-peak gradient >20 mm Hg or mean Doppler systolic gradient >20 mm Hg.

Catheter interventional techniques for recurrent aortic arch obstruction. The method of balloon angioplasty of aortic arch obstruction did not differ significantly from the procedure of primary dilatation. A percutaneous femoral artery approach was used in all the patients. A pigtail or a multipurpose catheter was passed through the arterial sheath, placed above narrow segment, pressure gradient was measured, and angiography was performed in two views. Indications for balloon angioplasty were transcatheter systolic gradient of >20 mm Hg and suitable anatomy. Appropriate sized balloon angioplasty catheter was selected. The balloon catheter was then passed over the guidewire and positioned across the narrow segment. The balloon was inflated to a pressure of 3 to 5 atm and kept inflated for 5 to 10 seconds. After performing a control assessment of hemodynamics and aortography, a decision was made regarding further tactics. When achieving the optimal result, according to aortography, and measuring the pressure in the ascending and descending aorta, repeated inflation of the balloon at the site of narrow segment was not performed.

Surgical technique. Several different surgical techniques for recurrent aortic arch obstruction were used (Table 2). The particular technique was chosen by the surgeon individually for each patient.

Lateral thoracotomy was used for relief of aortic obstruction in 11 patients. Thoracotomy was chosen because the narrow segment was distal enough to be safely addressed by thoracotomy. Surgical approach did not differ significantly from a primary aortic arch repair. A posterolateral thoracotomy was performed in the third intercostal space. Intrathoracic adhesions were divided paying much attention to the mobilization of vagus and recurrent laryngeal nerves. The aortic arch, left subclavian artery and descending thoracic aorta were dissected from their surrounding adhesions. The vascular clamp was placed directly near the brachiocephalic trunk in the area of proximal aortic arch, partially clamping the ascending aorta. At the same time, invasive pressure on the right radial artery was controlled, which is an indicator of adequate blood flow to the right common carotid artery. Distally, the clamp was placed on the descending thoracic aorta below the previous repair site. The narrowing segment was excised, longitudinal incision was made in the posterior wall of the descending aorta and then aortic arch repair was performed.

In the remaining 9 patients, reintervention was performed through a median sternotomy under cardiopulmonary bypass with antegrade cerebral perfusion. After starting cardiopulmonary bypass, the patient was cooled to 24-25 °C. The arterial cannula was then inserted into the brachiocephalic trunk and selective antegrade cerebral perfusion was initiated, reducing the volume perfusion rate to 30–40 % of normal. To prevent air embolism of cerebral vessels, the tourniquets were pulled tightly around aortic cannula, left carotid and subclavian arteries. The incision of the aortic arch was performed in the longitudinal direction from descending to ascending aorta and then aortic arch repair was performed.

The main surgical technique used to relieve recurrent aortic arch obstruction was extended end-to-end anastomosis (n = 10). The aortic arch was mobilized, narrow segment was excised and aorta was anastomosed in an end-to-end fashion. Autologous pericardial patch aortoplasty was used in 6 patients including patch extension into the proximal arch in every case. One patient underwent aneurysm resection and xeno-pericardial patch repair.

Statistical analysis. Statistical analyses were performed using the Microsoft Excel 2016, IBM SPSS Statistics 21.0. Freedom from aortic arch reintervention secondary to aortic arch reobstruction was estimated using Kaplan-Meier curves. To find risk factors for reintervention, Cox regression analyses with all available anatomic, presurgical and surgical variables were performed. P-value <0.05 was accepted as a statistically significant difference.

Results. The hospital mortality after primary aortic arch repair in infants was 2.7 % (n = 12), mortality in the long term was 0.7 % (n = 3). Analysis of the hospital mortality showed that only one patient died with isolated aortic arch hypoplasia, all others had associated congenital heart disease. It should also be noted that only in one patient the cause of death was ineffective aortic arch repair, resulting in the development of heart failure. In other patients, the reasons were related to associated cardiac defects repair.

Follow-up period ranged from 1 month to 9.4 years (mean 2.8 ± 2.5 years). Restenosis at the site of aortic arch repair was identified in 47 (10.5 %) patients. Of these, 12 patients underwent surgical reconstruction of the aortic arch, 27 patients underwent balloon angioplasty, and in 8 patients both methods were used. A total of 58 reinterventions were required for restenosis. Median interval from primary arch repair to reintervention for recurrent aortic obstruction was 8.4 ± 1.2 months. Of the 47 patients who underwent reintervention on the aortic arch, 17 (36.1 %) patients weighed less than 2500 g.

Hospital mortality after surgical repair of recurrent aortic arch obstruction was 2.1 % (n = 1). Mortality was not associated with the technique of reintervention on the aortic

Table 2

Surgical techniques used for recurrent aortic arch obstruction

Surgical technique	Lateral thoracotomy n = 11	Median sternotomy n = 9
Extended end-to-end anastomosis	8	2
End-to-side anastomosis	–	1
Amato technique	2	–
Autologous pericardial patch aortoplasty	–	6
Aneurysm resection	1	–

arch. The cause of death was acute heart and respiratory failure associated with the correction of other congenital heart disease. There were no late deaths. The main characteristics and outcomes for patients who underwent aortic arch reconstruction are described in Table 3.

At the time of reintervention, the median systolic gradient across the obstruction was 50.8 ± 17 mm Hg. According to echocardiography after reintervention, the median systolic gradient significantly decreased to 13 ± 4 mm Hg (P <0.05).

The recurrent aortic arch obstruction was located at the isthmus in 10 patients, at the isthmus and the distal aortic arch in 8, and at the distal and proximal arch in 29 patients. The obstruction was discrete in 27 patients and was suitable for balloon dilatation. In all the patients, immediate result after reintervention was successful, with the pressure gradients after reintervention less than 20 mm Hg. Increase in isthmus, distal and proximal arch Z-score was found in all the patients. Median follow-up after reinterventions was 2.8 ± 2.5 years. A second reintervention was performed in 11 patients: 5 patients after balloon angioplasty (3 patients underwent second balloon angioplasty, 3 patients had patch enlargement) and 6 patients after surgical reintervention (4 patients underwent balloon angioplasty, 3 patients had second surgical reintervention).

In multivariable analysis, independent risk factors for reintervention due to restenosis were hypoplastic proximal aortic arch (P = 0.002) and body weight less than 2500 g (P = 0.004) at primary repair (Table 4).

The Kaplan-Meier estimate of freedom from reintervention was 89.4 % at 1-year follow-up and 87.5 % at 4-year follow-up (Fig. 2).

Discussion. Restenosis rate and reinterventions after aortic arch repair in infants are still a matter of concern. The rate of restenosis in our study is 10.5 % in patients who underwent surgery, which was comparable to the results from other studies [8, 10]. There has been much debate re-

Table 3

Patient characteristics and outcomes of aortic arch reinterventions

Characteristics	Before reintervention	After reintervention	Before discharge
Age, months	1.3 ± 0.4	5.8 ± 3.0	5.8 ± 3.4
Weight, kg	4.0 ± 2.0	5.9 ± 2.7	5.9 ± 3.2
Z-score, aortic isthmus, mean ±SD	–5.9 ± 1.7	–2.7 ± 1.2	–1.3 ± 0.4*
Z-score, distal aortic arch, mean ±SD	–3.1 ± 1.4	–2.2 ± 0.9	–1.4 ± 0.8*
Z-score, proximal aortic arch, mean ±SD	–3.1 ± 1.1	–2.7 ± 1.0	–1.6 ± 0.3*
Mean systolic gradient, mm Hg	45 ± 18	50.8 ± 17	13 ± 4*
LVEF (%)	61 ± 12	64 ± 10	67 ± 4

* P-value <0.05.
LVEF, left ventricular ejection fraction.

Table 4

Analysis of risk factors for aortic arch reintervention

Predictor	B	P	Exp(B)	Exp(B) 95 % CI
Body weight <2500 g	2.769	0.004	15.94	2.39–106.49
Hypoplastic proximal aortic arch	3.635	0.002	37.91	3.91–367.99
Constant	–8.771	0.000	0.001	–

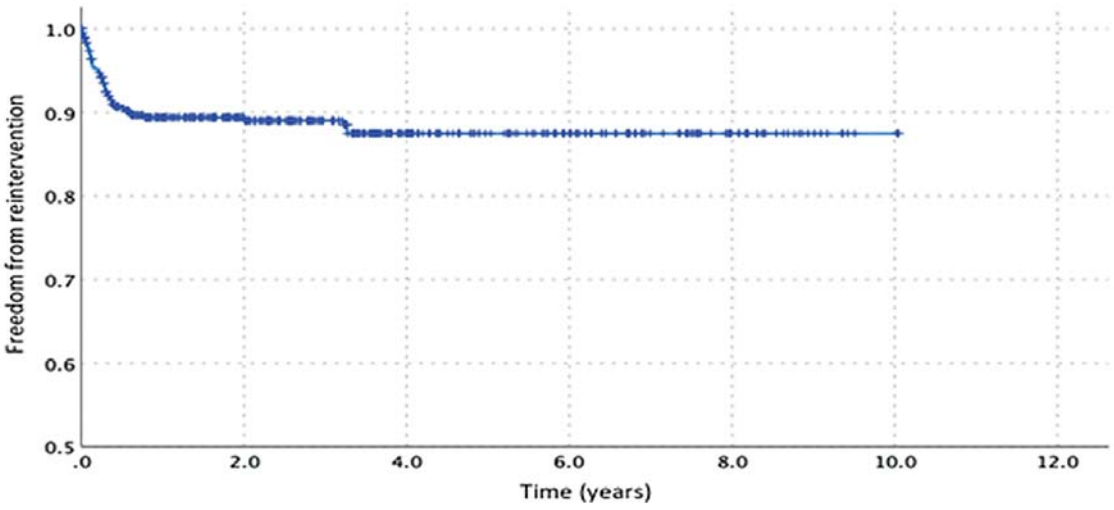

Fig. 2. *Freedom from reintervention after aortic arch repair in infants*

garding the risk factors for recurrent aortic obstruction. According to systematic review, risk factors for reobstruction of the aorta can be summarized in the following categories: demographic variables, associated anomalies, clinical and intervention variables, morphometric variables [11]. Low weight at intervention is classically viewed as a potential risk factor for restenosis [12, 13]. This is confirmed by several studies, showing a significant association between low body weight at the time of repair and arch restenosis. Bacha et al. identified that weight less than 1.5 kg at the time of primary arch is an independent predictor of recurrent aortic arch obstruction [14]. However, Sudarshan et al. and Jiang et al. noted that low weight was not a significant factor for choosing surgical strategy [15, 16]. Our study shows that weight less than 2500 g is indeed a risk factor for restenosis after neonatal aortic arch repair.

Some studies evaluating the association between restenosis and aortic arch morphometry showed that the hypoplastic aortic arch was a significant risk factor for recurrent aortic arch obstruction [17, 18, 19]. For example, McElhinney et al. measured the size of the aortic arch segments by echocardiography and concluded that the size of the transverse aortic arch is an important risk factor for restenosis after neonatal aortic arch repair [5]. Wu et al. also found that the size of the transverse aortic arch is a risk factor for recurrent aortic arch obstruction [20]. In the present study, we found that the diameter of the proximal aortic arch was associated with reintervention for recurrent aortic arch obstruction.

Concerning surgical technique, when possible, the reconstruction should be performed using native tissue. Many authors recommend an extended end-to-end or end-to-side anastomosis as the best method of primary hypoplastic aortic arch repair to avoid restenosis [21, 22, 23, 24]. In our study initial repair technique was not associated with recurrent aortic arch obstruction. As for surgical approach for reintervention, both median sternotomy and lateral thoracotomy were used. Surgical approach was chosen after a full preoperative examination including echocardiography, angiography, and magnetic resonance image scanning, and depended on the location and duration of reobstruction. In our opinion, if the narrowing aortic segment is located proximal to the previous repair site and if the transverse aortic arch remains significantly hypoplastic, the best surgical approach will be median sternotomy. If the recurrent obstruction is distal to the left subclavian artery, we used left thoracotomy.

The purpose of any reintervention after the initial reconstruction of the aortic arch is to completely eliminate the obstruction for further growth of all segments of the aortic arch, minimizing the risk of re-narrowing. Different methods are used to treat recurrent aortic arch obstruction: endovascular interventions (balloon dilatation, stenting), surgical techniques (extraanatomic bypass with synthetic vascular prostheses, anatomic aortic arch). Regarding the treatment strategy, surgical repair of recurrent aortic arch obstruction is preferred in cases when the area of obstruction involves a longer segment of obstruction [2, 25]. Balloon angioplasty has been increasingly used for local recurrent aortic obstruction and becomes the initial procedure of choice in many centers [9, 26]. Balloon dilatation of aortic arch restenosis demonstrates high efficiency of the procedure. Connective tissue at the site of primary surgical repair minimizes the risk of aneurysm formation after balloon dilatation. In our series, patients with suitable anatomy (locally narrowed segment) should have an initial trial of balloon angioplasty. This method was effective in the vast majority of patients with aortic arch restenosis.

Limitations. Whilst the number of investigated patients was high in our study, the main limitation of our study was retrospective approach. So, data are only available for the time when recurrent aortic arch obstruction was detected and not when it occurred. In addition, it was not possible to precisely analyze the anatomy of each aortic segment in all cases. This certainly limited identification of all anatomical risk factors for restenosis. Further study is necessary to describe the growth of the augmented aortic arch over time.

Conclusion. Aortic arch reobstruction is a common complication following aortic arch repair in infants. Both surgical and endovascular reinterventions after aortic arch repair in infants are safe, effective, and are associated with low incidence of restenosis. Freedom from reintervention was 89.4 % at 1-year follow-up and 87.5 % at 4-year follow-up. The most determining factors for restenosis were related to hypoplastic proximal aortic arch and body weight less than 2500 g.

Conflict of interest: the authors have nothing to declare.

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Частота рестенозів і повторні втручання після реконструкції дуги аорти у немовлят

Труба Я. П., д-р мед. наук, завідувач відділу хірургічного лікування вроджених вад серця у новонароджених та дітей молодшого віку

Головенко О. С., канд. мед. наук, провідний науковий співробітник відділення хірургічного лікування вроджених вад серця у новонароджених та дітей молодшого віку

Дзюрий І. В., лікар-кардіохірург відділення хірургічного лікування вроджених вад серця у новонароджених та дітей молодшого віку

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Резюме. Повторна обструкція залишається важливим ускладненням після реконструкції дуги аорти в немовлят. Оптимальні методи усунення повторного звуження залишаються суперечливими. В останні роки балонна дилатація рестенозів частіше використовується, однак у літературі деякі автори все ж рекомендують повторне хірургічне втручання, як більш ефективне для лікування повторного звуження в місці попередньої пластики дуги аорти. Серед прихильників хірургічної репластики дуги аорти, спірним питанням залишається методика реконструкції та хірургічний доступ.

Мета роботи – визначити частоту повторних втручань після реконструкції дуги аорти в немовлят, а також оцінити їх результати та проаналізувати фактори ризику реінтервенцій.

Матеріали та методи. У дослідження включено 445 новонароджених, яким з 2011 по 2019 рік у ДУ «Національний інститут серцево-судинної хірургії імені М. М. Амосова НАМН України» та ДУ «Науково-практичний медичний центр дитячої кардіології та кардіохірургії МОЗ України» проводили пластику дуги аорти внаслідок коарктації аорти з гіпоплазією дуги аорти. Критерії виключення: діти з одношлуночковою фізіологією. Коарктація аорти з гіпоплазією дуги аорти спостерігалася як ізольована вада у 159 (35,7 %) пацієнтів, асоційована з іншими вадами серця у 286 (64,3 %) пацієнтів. Пацієнтів чоловічої статі було 284 (63,8 %), жіночої – 161 (36,2 %). Середній вік хворих на момент першої операції становив 2,3 ± 0,8 міс., середня маса тіла – 4,8 ± 1,9 кг. Повторні втручання на дузі аорти виконано 47 (10,5 %) пацієнтам, які становили основну групу дослідження. Усім пацієнтам проводили планову трансторакальну ехокардіографію. Анатомічний опис дуги аорти аналізували за даними ехокардіографії. Діагноз гіпоплазії дуги аорти встановлювали, якщо відхилення дистального та проксимального відділів дуги аорти за Z-score було менше або дорівнювало –2. Утворення аневризми аорти визначали, якщо діаметр аневризми в 1,5 раза перевищував діаметр низхідної аорти на рівні діафрагми. Статистичний аналіз проводили за допомогою Microsoft Excel 2016, IBM SPSS Statistics 21.0. Свободу від повторних втручань на дузі аорти внаслідок повторної обструкції дуги аорти у віддаленому періоді проводили за допомогою кривих Каплана – Майєра. Для визначення факторів ризику повторного втручання, було проведено регресійний аналіз Кокса з усіма доступними анатомічними, передопераційними та хірургічними змінними. Р-значення < 0,05 було прийнято як статистично значуща різниця.

Результати. Госпітальна летальність після первинної пластики дуги аорти у немовлят становила 2,7 %, летальність у віддаленому періоді – 0,7 %. Аналізуючи госпітальну летальність, необхідно відзначити, що лише один хворий помер з ізольованою гіпоплазією дуги аорти, у всіх інших спостерігалися супутні вроджені вади серця. Слід також зазначити, що лише в одного хворого причиною смерті стала неефективна пластика дуги аорти, що призвело до розвитку серцевої недостатності. В інших пацієнтів причини були пов'язані з корекцією супутніх вад серця.

Період спостереження коливався від 1 місяця до 9,4 року (в середньому 2,8 ± 2,5 року). Рестеноз у місці пластики дуги аорти виявлено у 47 (10,5 %) пацієнтів. З них: 12 пацієнтам проведено хірургічну реконструкцію дуги аорти, 27 пацієнтам – балонну ангіопластику, у 8 пацієнтів використали обидва методи. Загалом було виконано 58 повторних втручань для усунення рестенозу дуги аорти. Середній інтервал від первинної корекції дуги до повторного втручання з приводу рецидиву обструкції аорти становив 8,4 ± 1,2 місяця. З 47 хворих, яким виконано повторне втручання на дузі аорти, 17 (36,1 %) хворих мали масу тіла менше ніж 2500 г.

Госпітальна летальність після хірургічного лікування рецидиву обструкції дуги аорти сягала 2,1 % (n = 1). Летальність не була пов'язана з технікою повторного втручання на дузі аорти. Причиною смерті стала гостра серцево-судинна та дихальна недостатність, пов'язана з корекцією супутніх вроджених вад серця. Летальних випадків у віддаленому періоді не відзначено.

Висновки. Рестеноз дуги аорти є поширеним ускладненням після реконструкції у немовлят. Як хірургічні, так і ендоваскулярні повторні втручання після пластики дуги аорти в немовлят є безпечними, ефективними та мають низьку частоту рестенозів. Свобода від повторних втручань через 1 рік спостереження становила 89,4 %, через 4 роки – 87,5 %. Найбільш визначальними факторами виникнення рестенозу були гіпоплазія проксимальної дуги аорти та маса тіла менше ніж 2500 г.

Ключові слова: *повторна обструкція, балонна ангіопластика, хірургічна реконструкція, фактори ризику летальності, гіпоплазія.*

Стаття надійшла в редакцію / Received: 02.11.2022
Після доопрацювання / Revised: 11.11.2022
Прийнято до друку / Accepted: 10.12.2022