AUCTORES
Globalize your Research

Cardiology Research and Reports
Mariela Céspedes Almira *

Open Access

Research Article

Algorithm for diagnosis and typing of ALCAPA syndrome.

Mariela Céspedes Almira MD. MSc[1*], Adel Eladio González Morejón MD. PhD. FACC[1], Giselle Serrano Ricardo MD. PhD[1], Tania Rosa González Rodríguez MD. MSc[1], Judith Escobar Bermúdez MD[2]

[1]Specialist in Pediatric and Cardiology. Professor and Researcher, Pediatric Cardiocenter William Soler, Havana Cuba.

[2]Specialist in Pediatric. Professor, Pediatric Cardiocenter William Soler, Havana Cuba.

***Corresponding author:** Mariela Céspedes Almira, Institute of Clinical Medicine. Tbilisi. Georgia.

Received Date: April 05, 2021; Accepted Date: April 16, 2021; Published Date: April 21, 2021.

Citation: Mariela C Almira, Adel E G Morejón, Giselle S Ricardo, Tania R G Rodríguez, Judith E Bermúdez. (2021) Algorithm for diagnosis and typing of ALCAPA syndrome. Cardiology Research and Reports. 3(2): Doi: 10.31579/2692-9759/020

Abstract

ALCAPA syndrome was characterized by anomalous origin of left coronary artery from pulmonary artery. Its clinical presentation is varied and although it is an anomaly of congenital origin, it is not exclusive to pediatric ages. Its epidemiological documentation is difficult. We aimed to make the non-invasive diagnosis of the ALCAPA syndrome and its variants.

An observational, prospective and cross-sectional study was conducted with 31 patients with a positive echocardiographic diagnosis of ALCAPA syndrome at Pediatric Cardio Center "William Soler" from 2005 to 2018.

The variables with significance for diagnosis were the echocardiographic visualization of the anomalous connection and the reversed flow in the left coronary artery. The variables with significance for typing were age at diagnosis, ischemia in the electrocardiogram, echocardiographic visualization of left ventricle papillary muscles fibrosis, presence of severe mitral regurgitation, left ventricle spheroidal remodeling, left ventricle ejection fraction, left ventricular end-diastolic volume index, and left ventricular end-diastolic diameter index. An algorithm integrated by various diagnostic modalities associated with echocardiography as a tool for the detection of ALCAPA was developed.

The documentation of the diagnostic and classificatory aspects of the syndrome is possible by detecting echocardiographic elements in conjunction with electrocardiographic and radiological aspects.

Keywords: ALCAPA syndrome; anomalous coronary artery; diagnosis; echocardiography

Introduction

Coronary abnormalities are an infrequent but transcendent cause of chest pain, myocardial ischemia and sudden death [1], the latter, which is often the only symptom [2, 3]. Coronary artery abnormalities have an incidence in the general population of 0.2 to 1.2 %. The origin of left coronary artery from the pulmonary artery is the most frequent, also known in the literature as ALCAPA (Anomalous Left Coronary Artery from the Pulmonary Artery) [4, 5]. The syndrome represents from 0.25 % to 0.5 % of all documented congenital heart diseases in extrauterine life [6-9].

The pioneering diagnosis of this coronary anomaly was based on the findings from the autopsy. The early postulate of Brooks [10] regarding the existence of unusual blood flow within the pulmonary artery from coronary vessels was not corroborated by the results of the right heart catheterization, which, at that time, was unable to detect the connection anomaly of left coronary artery with the pulmonary artery. However, later the afore mentioned contrasted study became the diagnostic means of choice for the disease. The late twentieth century and the dawn of the twenty-first century contemplate the emergence and technological development in the fields inherent to computed tomography and cardiac magnetic resonance imaging that, in conjunction with the indirect findings of suspicion from echocardiography, have allowed the evaluation non-invasive coronary anatomy and increased reports of cases afflicted by the condition in adult patients [11-13].

The clinical expression of ALCAPA is diverse and nonspecific; patients may be asymptomatic or present with dyspnea, angina, fatigue, and palpitations. Progressive heart failure and mitral regurgitation, ischemic cardiomyopathy, diffuse endomyocardial fibroelastosis of the left ventricle, dilated cardiomyopathy, pulmonary hypertension and malignant ventricular arrhythmias (80 % to 90 % of patients) precipitated by exercise capable of causing sudden death, a situation that occurs in asymptomatic patients generally in the third decade of life [14-16].

The plurality in the behavior of the syndrome with respect to the possibilities of clinical detection and at the time of presentation was related to the pathophysiological changes that accompany the fetus, the newborn and the infant. Adult patients with ALCAPA adapt to chronic ischemia, poor perfusion, and arterial-venous shunting. The lack of these adaptations contributes to morbidity and mortality. Chronic ischemia produces left ventricular systolic dysfunction and ventricular dilation. The

most affected area is the anterolateral wall of the left ventricle and the homonymous mitral papillary muscle, two of the elements on which the presentation is based [17].

The afore mentioned syndrome occurs in two variants (infantile or adult), independent of the age of debut, that is, it is not exclusive to pediatric age despite constituting a congenital anomaly and there are differences in the clinical, electrical and imaging findings [9].

The early diagnosis of this disease determines its prognosis and allows the modification of its natural history through surgery [18-20]. Surgery slows down or stops the dynamic ischemic process attributable to the disease.

The clinical method is not sufficient for the detection of this congenital anomaly. Echocardiography, faced with the scrutiny of a large number of subjects, is the ideal tool to solve the problem mentioned and promote the diagnosis, on objective and reliable bases, of individuals with the condition who are “masked” or “silent”.

The objective of this research is to establish patterns to detection of patients suffering from the anomaly with the use of echocardiography as a useful tool for population research focused on the diagnosis and typification of the ALCAPA syndrome. We propose an algorithm that improve a diagnostic in such complex health problems.

Methods

This was an observational, prospective and cross-sectional study at a single tertiary care center. We included 31 patients of both sexes with a positive echocardiographic diagnosis of ALCAPA monitoring in the Pediatric Cardio Center “William Soler”, in the period comprised from 2005 to 2018.

The hospital where the research was developed is a national reference center for the diagnosis, treatment and monitoring of patients with congenital heart disease, which justifi es the possibility of studying all subjects.

The research was based on the analysis of various clinical, electrical, radiological and echocardiographic variables that have been conceptually defined [21-22]. As dependent or response variables were included the diagnosis and typification of the ALCAPA syndrome. As independent or explanatory variables were included for diagnosis the echocardiographic visualization of the anomalous connection, reversed flow in the anomalous coronary artery, location of the anomalous left coronary artery, coronary artery dilatation and increased coronary collateral vascularization. Were included for typing: ischemia in the electrocardiogram, cardiothoracic index, left ventricle spheroidal remodeling, left ventricle papillary muscles fibrosis, the presence of severe mitral regurgitation, left ventricular end-diastolic diameter index (LVEDD index), left ventricular end-diastolic volume index (LVEDV index) and left ventricular ejection fraction (LVEF). Age and gender as control variables.

The information was obtained from the anamnesis, physical examination and echocardiographic investigation, collected and recorded in two models, a census model for the population of sick individuals and a survey for supposedly healthy subjects, with a structure a database capable of being used by the free statistical platform R Project 3.0.1.

As a single experienced cardiologist performed echocardiographic examinations of all patients, a third-party blinded study was performed to avoid bias.

The statistical analysis was based on the application of a logistic regression model with which it was intended to evaluate the relationship and independent influence of each variable on the possibility of making the diagnosis and typing by echocardiography of the ALCAPA syndrome. The independent variables were made up of those that, according to the research findings, were considered as prone to diagnosis and typification of the disease under study. The quantitative variables were coded for their introduction in the model analysis process; This considered identifying, as elements that generate influences on the predetermined dependent variables, those aspects for which the Wald statistician showed probability less than 5 % ($p < 0.05$) when the exponential of the model coefficients was analyzed (Exp ß) as an estimator of the ratio of cross products or Odds ratio (OR).

The goodness of fit corresponding to the proposed model was determined using the Hosmer and Lemeshow test, which allowed evaluating the value of the deviation between it was observed and it was expected, integrated by the evaluation by Chi-squared (X^2) and by the coefficients of determination R^2 of Cox and Snell and Nagelkerke's R^2, which indicate the variance of the dependent variable explained by the model.

The present study was carried out in accordance with the precepts and strict compliance with the Declaration of Helsinki [23].

Results

Table 1 showed the logistic regression that identifies the facilitating variables of the echocardiographic diagnosis in the ALCAPA syndrome. The echocardiographic visualization of the anomalous connection and the detection of reversed flow in the anomalous coronary artery were the only variables that presented absolute statistical significance as useful elements for the effective diagnosis of the disease ($p < 0.001$).

Table 2 demonstrated the result that emanates from the multivariate analysis at the starting point of the logistic regression carried out to identify the aspects that influence or determine the echocardiographic typification of the ALCAPA syndrome used, the latter, as the dependent variable in the present model. Documentation of differences regarding age at diagnosis (Exp β - 2,699; Wald - 4,812; p 0.043), the presence of (Exp β - 36,108; Wald - 7,415; p 0,005), the existence left ventricle papillary muscles fibrosis (Exp β - 21.457; Wald - 5.986; p 0.01), the detection of severe mitral regurgitation (Exp β - 15.106; Wald -5.710; p 0.019) and the identification of the left ventricle spheroidal remodeling (Exp β - 21.465; Wald - 5.992; p 0.013) are part of the set of independent variables that define the afore mentioned typing. Also included ischemia in the electrocardiogram in this group are the perception of quantitative differences corresponding to the ejection fraction (Exp β - 1,998; Wald - 4,361; p 0.031), the end-diastolic volume index (Exp β - 21,300; Wald - 5,872; p 0,015) and the end-diastolic diameter index (Exp β - 15.714; Wald - 5.971; p 0.014) in the left ventricle.

The goodness of fit corresponding to the proposed model because of the logistic regression carried out was determined using the Hosmer and Lemeshow test. Table 3 showed that the analysis of the test statistician in the studied population did not present statistical significance (p 0.81) or differences between predicted and observed, so the proposed model was valid.

The application of the Hosmer and Lemeshow test to the model built based on multivariate analysis incorporated the coefficient of determination (R^2) of Cox and Snell, as well as its corrected version of Nagelkerke in order to document the proportion of variance corresponding to the dependent variable according to its independent counterparts. The findings, which are shown in Table 4, denoted that the mentioned model was able to predict the exact typing in 88.2 % of the patients with the infantile-type and 78.5 % of the subjects afflicted by the adult-type of the disease. The general quantification of success, in percentage terms, to 83.3 %. The resulting figures from the Cox and Snell coefficient of determination (0.317) and its corrected version (0.424) support the clinical application of the model obtained.

Variables	p	Exp (β). OR Estimate	Wald
Echocardiographic visualization of the abnormal connection	0.000	-	-
Lateral location of the anomalous left coronary artery	0.775	1.233	0.104
Reverse flow in the abnormal coronary artery	0.000	-	-
Increased coronary collateral vascularization	0.069	3.321	3.315
Right coronary artery dilation	0.981	0.000	0.000

Table 1: Identification of the variables that facilitate echocardiographic diagnosis of ALCAPA syndrome.

Variables	p	Exp (β). OR Estimate	Wald
Age at diagnosis Infantile-type (up to three years) Adult-type (older than three years)	0.043	2.699	4.812
Electrocardiographic. Ischemia signs Infantile-type (present) Adult-type (absent)	0.005	36.108	7.415
Left ventricle papillary muscles fibrosis Infantile-type (present) Adult-type (absent)	0.01	21.457	5.986
Severe mitral regurgitation Infantile-type (present) Adult-type (absent)	0.019	15.106	5.710
Cardiothoracic index Infantile-type (> 0.59) Adult-type (until 0.56)	0.986	0.000	0.000
Left ventricle spheroidal remodeling Infantile-type (present) Adult-type (absent)	0.013	21.456	5.992
Left ventricular ejection fraction Infantile-type (until 30.0 %) Adult-type (> 57.7 %)	0.031	1.998	4.361
Left ventricular end-diastolic volume index Infantile-type (> 71.02 ml / m^2) Adult-type (until 87.8 ml / m^2)	0.015	21.300	5.872
Left ventricular end-diastolic diameter index Infantile-type (> 93.1 mm / m^2) Adult-type (until 53.4 mm / m^2)	0.014	15.714	5.971

Table 2: Identification of the variables that facilitate echocardiographic typing of the ALCAPA syndrome.

Quartiles	Typing of the ALCAPA syndrome				Total
	Infantile-type		Adult-type		
	Observed	Expected	Observed	Expected	
1	4	5.250	2	.750	6
2	3	3.937	3	2.063	6
3	5	5.562	1	.438	6
4	1	.438	5	5.562	6
5	0	.000	2	2.000	2

$P \geq 0.81$

Table 3: Hosmer and Lemeshow test. Contingency table obtained after the modeling process carried out.

Observed results	Predicted Results		Percentage correct
	Infantile-type	Adult-type	
Infantile-type (N = 17)	15	2	88.2
Adult-type (N = 14)	3	11	78.5
Overall percentage			83.3 §
Coefficient of determination			Results
R^2 de Cox y Snell			0.317
R^2 de Nagelkerke			0.424

§ Hosmer and Lemeshow test
X^2 Test 3.720. p 0.81

Table 4: Goodness of fit corresponding to the proposed model by logistic regression.

In order to establish useful strategies for the population research focused on the diagnosis in conjunction with the typification of the ALCAPA syndrome, an algorithm integrated by various diagnostic modalities associated with echocardiography as an initial, precise and fundamental tool was developed. The algorithm can be seen in Figure 1.

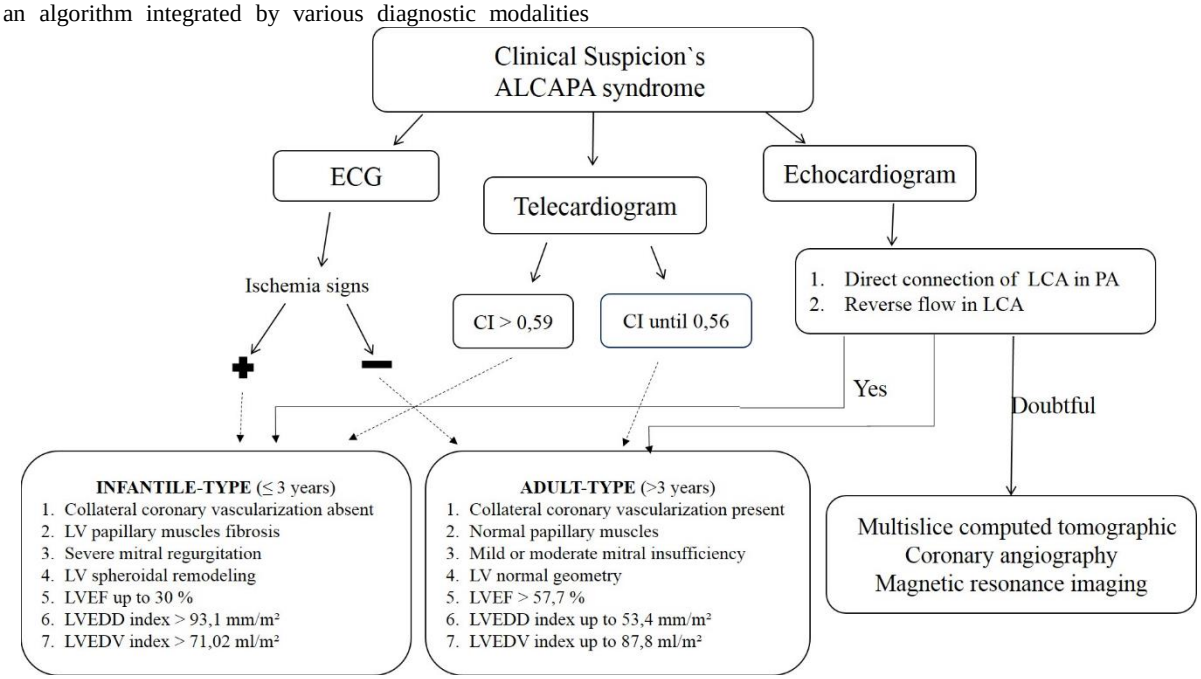

Figure 1: Diagnostic algorithm for ALCAPA syndrome

Discussion

The medical literature that addresses the general aspects inherent to the ALCAPA syndrome establishes some non-invasive diagnostic criteria of the condition that was based on the ambiguous observation of indirect echocardiographic signs and identifies two variants of the disease that are well defined from the conceptual point of view, although does not establish the methodology for differentiation through the applicability of non-invasive modalities [24-27].

Other imaging techniques such as computerized axial tomography, magnetic resonance imaging and cardiac catheterization can demonstrate the coronary abnormality; however, these diagnostic modalities are not very accessible, exhibit high cost and require optimization during the inherent process of image acquisition [28-33].

Logistic regression is the direct probability model that integrates the set of so-called dependency techniques that have explanatory or predictive capacity of a phenomenon defined by a variable that acts as a dependent depending on some factors that are related to it and that interact as independent variables (explanatory or predictive) [34-36]. The logistic regression model identifies the group of probable risk factors for the occurrence of the dependent variable studied.

In the present investigation, the statistical processing determined that the visualization of the anomalous connection belonging to the left coronary artery and the detection of reversed blood flow inside the mentioned vessel have absolute value for the echocardiographic diagnosis of the ALCAPA syndrome.

Ya - Li Yang et al. agree with the postulates emanating from the present investigation by relating the direct visualization of the anomalous connection corresponding to the left coronary artery and the detection of reversed blood flow inside the mentioned vessel with the echocardiographic diagnosis of ALCAPA syndrome [37].

The conjugation of the clinical state documented in each patient with the electrocardiographic and radiological findings can facilitate, in a limited

way, the establishment of the differential analysis between types of the disease under study [17, 38-40]. Age as an absolute element of judgment for the typification of the ALCAPA syndrome lacks value since both classificatory variants can be expressed in pediatric patients [41-43].

There are several useful studies as cognitive elements of the symptoms found in groups of patients of different ages who are afflicted by the ALCAPA syndrome. Yau et al. report in a descriptive way, a set of patients detected in adulthood; of these, 12 % had a silent course during life and were classified as necropsy findings, 66 % had symptoms of angina, dyspnea, palpitations or fatigue, and 17 % suffered from ventricular arrhythmia, syncope states or episodes of sudden death [11].

Congenital heart disease in adulthood is associated with heart failure, arrhythmias, vascular complications, and sudden death [11, 14]. Many of these diagnoses are made, in this age group, incidentally, due to concomitant heart disease and sometimes, due to the presence of symptoms that lead to the finding of the lesion. When performing an echocardiographic study in an adult patient with signs and symptoms of heart failure, consider congenital heart disease [12, 13, 44].

According to the hypothesis raised by the present investigation, echocardiography stands as the ideal diagnostic modality in the capacity to integrate and enrich the concepts exposed in the face of the afore mentioned diagnostic ambiguities generated by the condition.

The identified results are compatible with the stated postulates.

The group of patients classified as belonging to infantile-type was made up of younger subjects when the condition was detected by echocardiography; these patients presented a predominance of the typical ischemic electrocardiographic pattern and were clinically expressed as individuals suffering from suspected dilated cardiomyopathy or severe isolated mitral regurgitation. Echocardiographic investigation of the left ventricle detected final diastolic dilation, spheroidal remodeling, left ventricle papillary muscles fibrosis, and global contractile dysfunction; these findings were accompanied by the cardiomegaly documented in the radiographic studies performed.

The patients with the adult-type of the syndrome were older at the time of echocardiographic diagnosis, which, at the same time, revealed the extensive existing collateral coronary vascular network. In these subjects, it was not possible to document processes tending to ventricular remodeling, the presence left ventricle papillary muscles fibrosis, global contractility disorders, or left ventricle final diastolic dilation. The radiographic study performed did not show cardiomegaly.

The logistic regression and its model, built from the independent variables identified as presumed classificatory elements, constituted the tools applicable to the multivariate analysis aimed at the typification of the ALCAPA syndrome adopted, the latter, as a dichotomous dependent variable. The figures set for the quantitative variables that were integrated into the model were adopted according to the values recorded by the standard deviations or the interquartile range used as measures of dispersion according to the examination corresponding to the intrinsic distribution of each variable in question. Afore mentioned statistical process allowed the finding of notable differences between both types related to age at diagnosis of the anomaly, presence of ischemia in the electrocardiogram, existence of left ventricle papillary muscles fibrosis, detection of insufficiency mitral injury, presence of elements tending to left ventricle spheroidal remodeling, left ventricular ejection fraction, left ventricular end-diastolic volume index, and left ventricular end-diastolic diameter index.

The information provided by the goodness-of-fit analysis corroborates the accuracy of the model in terms of echocardiographic typing of the ALCAPA syndrome.

In patients with cardiac symptoms of any age group, it is important to exclude the presence of ALCAPA. The conjugation of the clinical manifestations (unexplained crying spells in young infants, cardiomegaly, murmur of mitral regurgitation, dilated cardiomyopathy, myocardial ischemia, sudden death, arrhythmias, chest pain, myocarditis, coronary fistulas), with the electrocardiographic, radiological and echocardiographic findings can facilitate the diagnosis of this anomaly.

Conclusions

Echocardiographic visualization of the anomalous origin of the left coronary artery from pulmonary artery and the detection of local intracoronary reverse flow are the factors to be consider for the effective diagnosis of the disease. Non-invasive characterization of each variant of the ALCAPA syndrome is possible by detection of well-defined echocardiographic elements in conjunction with some electrocardiographic and radiological aspects.

Conflict of interests

The authors declare that they have no conflict of interest in conducting the study.

Authorship

Mariela Céspedes Almira: conception, design of the study and preparation of the draft of the article.

Adel Eladio González Morejón: analysis and interpretation of data, critical review of the article, approval of the final version.

Giselle Serrano Ricardo: critical review of the article, contributions to its intellectual content.

Tania Rosa González Rodríguez: contributions to its intellectual content.

Judith Escobar Bermúdez: contributions to its intellectual content.

References

1. Xiao Y, Jin M, Han L, Ding W, Zheng J, Sun C, et al. (2014) Two congenital coronary abnormalities affecting heart function: Anomalous origin of the left coronary artery from the pulmonary artery and congenital left main coronary artery atresia. Chin Med J. 127:3724-3731.
2. López Hloska NA, Zuloaga M, Rivero WG, Villasis A, Basualdo F, Carrizo MN, et al. (2019) Síndrome de Bland-White-Garland. Rev CONAREC. 34:109-111.
3. Harmon KG, Asif IM, Maleszewski JJ, Owens DS, Prutkin JM, Salerno JC, et al. (2015) Incidence, cause and comparative frequency of sudden cardiac death in national collegiate athletic association athletes: a decade in review. Circulation. 132:10-19.
4. Queiroz de França JC, Fernandes de Godoy M, Ribeiro Spotti M, Antonio dos Santos M, Correa Pivatelli F, Guimarães Neto WP. (2018) Larga supervivencia en paciente con síndrome de ALCAPA no corregido. Presentación de un caso clínico y revisión de la literatura. Insuf Card. 13: 45-49.
5. Hernández-Madrid A, Paul T, Abrams D, Aziz PF, Blom NA, Chen J, et al. (2018) Arrhythmias in congenital heart disease: a position paper of the European Heart Rhythm Association, association for the European Paediatric and Congenital Cardiology and the European Society of Cardiology. Europace. 20:1719-1753.
6. Perloff JK. (2012) Anomalous origin of the left coronary artery from the pulmonary trunk. In: Perloff JK, Marelli AJ editors. Perloff 'S clinical recognition of congenital heart disease. Sixth ed. Philadelphia: Elsevier.p.394-404.
7. Bachini JP, Amodio A, Guzmán R, Fernández N, Ivanna Duro I, Viñas S. (2019) Nacimiento anómalo de la arteria coronaria

izquierda desde la arteria pulmonar, síndrome de ALCAPA. Primer reporte de caso en Uruguay. Rev Urug Cardiol. 34:213-217.
8. Ramírez RF, Bitar HP, Paolinelli GP, Pérez CD, Furnaro F. (2018) Anomalías congénitas de arterias coronarias, estudio de aquellas con importancia hemodinámica. Rev Chil Radiol. 24:142-150.
9. Céspedes Almira M, Serrano Ricardo G, González Morejón AE. (2016) Síndrome de Bland, White y Garland. Rev Cub Ped. 88:205-213.
10. Brooks HS. (1885) Two cases of an abnormal coronary artery of the heart arising from the pulmonary artery. J Anat Physiol. 20:26-29.
11. Yau JM, Singh R, Halpern EJ, Fischman D. (2011) Anomalous origin of the left coronary artery from the pulmonary artery in adults: a comprehensive review of 151 adult cases and a new diagnosis in a 53-year-old woman. Clin Cardiol. 34: 204-210.
12. Li RJ, Sun Z, Yang J, Yang Y, Li YJ, Leng ZT, et al. Diagnosis value of transthoracic echocardiography in patiens with anomalous origin of the left coronary artery from the pulmonary artery. Medicine. 95:3401.
13. Takemoto K, Hirata K, Tanimoto T. (2015) Combined non-invasive doppler echocardiography and coronary computed tomography lead to diagnosis of anomalous left coronary artery from the pulmonary artery (ALCAPA) syndrome. Circ J. 79:1136-1138.
14. J. Kothari, K. Lakhia, P. Solanki, D. Parmar, H. Boraniya, S. Patel. (2016) Anomalous origin of the left coronary artery from the pulmonary artery in adulthood: challenges and outcomes. Korean J Thorac Cardiovasc Surg. 49:383-386.
15. J.R. Boris, J.A. (2015) Brothers. Primary-care management of patients with congenital anomalies of the coronary arteries. Cardiol Young. 25:1540-1545.
16. N.H. Silverman. (2015) Echocardiographic presentation of anomalous origin of the left coronary artery from the pulmonary artery. Cardiol Young. 25:1512-1523.
17. Philip DA, Newby DE. (2019) Non-invasive imaging of the coronary arteries. Eur Heart J. 40: 2444-2454.
18. López LP, Centella Hernández T, López Menéndez J, Cuerpo Caballero G, Silva Guisasola J, Hornero Sos F. (2019) Registro de intervenciones en pacientes con cardiopatía congénita de la Sociedad Española de Cirugía Torácica-Cardiovascular 2017 y retrospectiva de los últimos 6 años. Cirug Cardiov. 26:28-38.
19. Cabrera AG, Chen DW, Pignatelli RH, et al. (2015) Outcomes of anomalous left coronary artery from pulmonary artery repair: beyond normal function. Ann Thorac Surg. 99:1342-1347.
20. Vilá Mollinedo LG, Jaime Uribe A, Aceves Chimal JL, Martínez-Rubio RP, Hernández-Romero KP. (2016) Case Report: ALCAPA syndrome: successful repair with an anatomical and physiological alternative surgical technique. F1000Research. 5:1-11.
21. Llerena Rojas LR, Llerena Rojas LD, Marcos Gutiérrez Y, Bencomo Rodríguez Ll. (2019) Apuntes e imágenes de radiología cardiovascular. La Habana: Editorial Ciencias Médicas;.p. 7-10.
22. Braunwald E, Libby P, Bonow RO, Mann DL, Zipes DP. (2016) editors. Braunwald´s Heart Disease: A Textbook of Cardiovascular Medicine. 8th ed. Philadelphia: Saunders Elsevier. p. 509-540.
23. World Medical Association (WMA). World Medical Association Inc. (2017) Declaration of Helsinki-Ethical Principles for Medical Research Involving Human Subjects.
24. Dluz Niewska N, Kostkiewicz M, Tomkiewicz PL, Krupiński M, Podolec J, Olszowska M, et al. (2017) Non-invasive techniques for the diagnosis of anomalous origin of the left coronary artery from the pulmonary artery in adult patients. Acta Cardiol.; 72:41-46.
25. Molaei A, Hemmati BR, Khosroshahi H, Malaki M, Zakeri R. (2014) Misdiagnosis of Bland- White- Garland syndrome: report of two cases with different presentations. J Cardiovasc Thorac Res. 6: 65-67
26. Patel SG, Frommelt MA, Frommelt PC, Kutty S, Cramer JW. (2017) Echocardiographic diagnosis, surgical treatment, and outcomes of anomalous left coronary artery from the pulmonary artery. J Am Soc Echocardiogr. 30: 896-903.
27. Wen-xiu L, Bin G, Jiang W, Min CH, Gui-zheng Z. (2014) The echocardiografphy diagnosis of infantile and adult types of anomalous origin of the left coronary artery from the pulmonary artery. Chin J Evid Based Pediatr.; 9:186-189.
28. Amaral ME, Epifanio P, Noronha N, Pires A, Martinsa P, Azevedo V, et al. (2019) Causa rara de disfunção ventricular esquerda em idade pediátrica. Rev Port Cardiol. 38: 159.
29. Yamanaka O, Hobbs R. (1990) Coronary Artery Anomalies in 126,595 patients undergoing Coronary Arteriography. Catheter Cardio Diag. 21: 2840.
30. Umairi RS, Kindi FA, Busaidi F. (2016) Anomalous origin of the left coronary artery from the pulmonary artery: the role of multislice computed tomography (MSCT). Oman Med J. 31: 387-389.
31. Schmitt B, Bauer S, Kutty S, Nordmeyer S, Nasseri B, Berger F, et al. (2014) Myocardial perfusion, scarring and function in ALCAPA: long-term analysis using MRI. Ann Thorac Surg. 98: 1425-1436.
32. Duan X, Yu T, Wang F, Liu H, Sun J, Zhai R. (2015) Anomalous origin of the left coronary artery from the pulmonary artery in infants: imaging findings and clinical implications of cardiac computed tomography. J Comput Assist Tomogr. 39:189-195.
33. Salerno M, Sharif B, Arheden H, Kumar A, Axel L, Li D, et al. (2017) Recent advances in Cardiovascular Magnetic Resonance: Techniques and applications. Circ Cardiovasc Imaging. 10:1-10.
34. López-Roldán P, Fachelli S. Análisis de regresión logística. (2016) En: Metodología de la investigación social cuantitativa [Internet]. Bellaterra: Universitat Autónoma de Barcelona.
35. Lapresa D, Arana J, Anguera T, Pérez-Castellaños JI, Amatria M. (2016) Aplicación de modelos de regresión logística en metodología observacional: modalidades de competición en la iniciación al fútbol. Anal. Psicol.; 32:288-294.
36. Rodríguez Rueda JM, González Ferrer V, Montero González TJ, Consuegra Carvajal AN. (2018) Regresión logística binaria para crear un modelo predictivo de daño hepático en el paciente séptico. Acta Médic Centro. 12:10-18.
37. Ya-Li Y, Navin CN, Xin-Fang W, Ming-Xing X, Qing L, Lin H, et al. (2007) Echocardiographic diagnosis of anomalous origin of the left coronary artery from the pulmonary artery. J Copilation. 24:405-411.
38. Haiyan Y, Jinqing L, Xiaojuan J. (2018) Diagnosis of anomalous origin of the left coronary artery from the pulmonary artery with echocardiography and digital subtraction angiography. C R Card. 2018:1-6.
39. Mondal PCh, Bera D, Gupta A, Tiwari S. (2015) ALCAPA presenting as acute coronary syndrome in an adult: an interesting case report with short review of literature. J Cardiovasc Dis Res. 6:40-44.
40. Preti A. (2018) Undiagnosed ALCAPA presentation at the preoperative anesthesia clinic. Anesthesiol Case Rep. 1:20-22.

41. Patrianakos AP, Hatzidakis A, Marketou M, Parthenakis FI. (2018) Adult-type ALCAPA syndrome: a rare coronary artery anomaly. Echocardiography. 35:1056-1059.
42. Fox SM. (2017) ALCAPA anomalous left coronary artery from the pulmonary artery. Pediatric EM. 3:9-12.
43. Levitas A, Krymko H, Ioffe V, Zalzstein E, Broides A. (2016) Anomalous left coronary artery from the pulmonary artery in infants and toddlers misdiagnosed as myocarditis. Pediatr Emerg Care. 32:232-234.
44. Bhatt A.B, Foster E, Kuehl K, Alpert J, Brabeck S, Crumb S, et al. (2015) Congenital heart disease in the older adult: a scientific statement from the American Heart Association. Circulation. 131:1884-1931.