Original Article

Surgical Outcomes of Anomalous Origin of the Left Coronary Artery from the Pulmonary Artery in Children: An Echocardiography Follow-up

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Abstract

Background: Anomalous origin of the left coronary artery from the pulmonary artery (ALCAPA) is a rare but potentially life-threatening congenital heart defect. A retrospective analysis was carried out to elucidate the surgical outcomes of ALCAPA in infants and children using follow-up echocardiography.
Methods: From September 2008 to March 2017, 26 children diagnosed with ALCAPA underwent left coronary re-implantation. All surviving patients received echocardiography during follow-up.
Results: The mortality rate after the operation was 11.5%. Before repair, twenty patients (76.9%) presented with left ventricular (LV) dysfunction. The mean *Z*-score of the preoperative LV end-diastolic diameter was 4.42 ± 2.09. Mitral regurgitation (MR) was present in all patients. Two patients (7.7%), both with mitral valve prolapse, underwent mitral valve repair at the time of ALCAPA repair. Two children required postoperative extracorporeal membrane oxygenation. LV function normalized at a median time of 5.3 months (range: 0.5–36.0 months). The *Z*-score of the LV end-diastolic diameter decreased simultaneously. The degree of MR gradually decreased in all surviving patients. All patients had patency of the proximal left coronary artery confirmed by echocardiography at the most recent follow-up. Six patients (26.1%) showed supravalvar pulmonary stenosis and seven patients (30.4%) showed right pulmonary stenosis during follow-up.
Conclusions: Coronary re-implantation was effective for rebuilding a dual coronary system in patients with ALCAPA and resulted in progressive improved LV function and reduced functional MR. Echocardiography was valuable for evaluating the outcomes. LV function, the degree of MR, and possible complications could be detected with follow-up echocardiography.

Key words: Anomalous Origin of the Left Coronary Artery from the Pulmonary Artery; Coronary Re-implantation; Echocardiography; Follow-up

Introduction

Anomalous origin of the left coronary artery from the pulmonary artery (ALCAPA) is a rare congenital anomaly. It occurs in approximately 1/300,000 live births and represents 0.5% of all congenital heart disease cases.[1] The majority of ALCAPA cases usually present in early infancy. With the decrease in pulmonary vascular resistance during the first few weeks of life, myocardial ischemia and/or infarction may occur. ALCAPA causes severe myocardial ischemia, global left ventricular (LV) dysfunction, and annular dilatation, producing various degrees of mitral regurgitation (MR). Patients with ALCAPA may present with congestive heart failure or cardiogenic shock. The clinical features depend on the degree of coronary artery collateral development.[2] Due to the lack of specificity in its clinical manifestations, ALCAPA might be misdiagnosed as dilated cardiomyopathy, endocardial fibroelastosis, or mitral valve lesions.[3] The early mortality rate can be as high as 90% if ALCAPA is not diagnosed and treated in a timely manner.[1]

Coronary re-implantation is performed to establish a dual coronary system. However, systematic assessments

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of the LV function and size, MR, and complications of patients with ALCAPA managed with left coronary artery (LCA) re-implantation are limited.[4] Although coronary computed tomography angiography, magnetic resonance imaging (MRI), and invasive angiocardiography are used for the diagnosis of ALCAPA, echocardiography still is harmless and inexpensive and is the most frequently used method at present. A retrospective analysis was conducted to elucidate the surgical outcomes of ALCAPA in infants and children using follow-up echocardiography.

Methods

Ethical approval

We presented our study to the Human Research Ethics Committee at Children's Hospital of Fudan University. Since it was a retrospective study and data analysis was performed anonymously, this study was exempt from ethical approval and the need to obtain informed consent from patients.

Patient population

Between September 2008 and March 2017, 26 children (9 males and 17 female), aged 45 days to 13.4 years with a median of 4.9 months, underwent repair of ALCAPA at Children's Hospital of Fudan University. Patient characteristics are summarized in Table 1. All the patients underwent direct LCA re-implantation.

Follow-up echocardiography

Transthoracic echocardiography was performed using an IE33 echocardiography system (Philips Medical Systems, USA) or Vivid7 echocardiography system (General Electric Company, USA). We focused on the end-diastolic volume (EDV), end-systolic volume (ESV), stroke volume (SV), ejection fraction of the left ventricle (LVEF), and the degree of MR. Routine two-dimensional parasternal long-axis and parasternal short-axis imaging were used to evaluate the EDV, ESV, SV, and LVEF. The severity of MR was graded using conventional guidelines.[5] The parasternal aorta short-axis view was estimated to obtain the origin and course of the LCA using cross-sectional imaging. Color Doppler flow imaging was used to observe the distribution of blood flow, especially after LCA re-implantation.

Statistical analysis

Data were analyzed using SPSS software (version 17.0; SPSS, Inc., Chicago, IL, USA). Descriptive statistics for continuous data were expressed as mean ± standard

Table 1: Characteristics of the patients with ALCAPA

Number	Age (months)/ gender	Weight (kg)	LCA origin from PA	Preoperative *Z*-score of LVEDD	Preoperative MVR	Preoperative LVEF (%)	Concomitant anomalies	Other information
1	1.5/male	5.0	Right posterior near bifurcation	3.52	Moderate	58	PFO	ECMO
2	1.7/female	4.3	Left posterior	3.80	Mild	48	PFO	Serial echo follow-up
3	2.0/male	4.6	Right posterior	5.55	Mild	50	N	Serial echo follow-up
4	3.0/male	5.0	Left-facing sinus	5.60	Moderate	27	PFO	ECMO Serial echo follow-up
5	3.2/male	4.8	Right pulmonary artery	3.39	Mild	42	CoA	Serial echo follow-up
6	3.5/female	5.0	Left posterior	7.12	Severe	30	N	Serial echo follow-up
7	4.0/female	5.8	Right posterior near bifurcation	6.65	Moderate	48	N	Serial echo follow-up
8	4.0/male	4.7	Right posterior	6.00	Moderate	45	PFO	Early dead
9	4.0/male	6.0	Right posterior	3.54	Moderate	51	N	Early dead
10	4.1/female	6.0	Right posterior	6.08	Moderate	28	N	Lately dead
11	4.2/male	6.0	Right posterior	6.62	Severe	38	PFO	Serial echo follow-up
12	4.5/female	5.0	Left posterior	7.70	Severe	38	PFO	Serial echo follow-up
13	4.8/female	5.5	Left posterior	6.87	Mild	35	PDA	Serial echo follow-up
14	5.0/female	6.0	Left posterior	5.21	Moderate	41	PFO	Serial echo follow-up
15	5.5/female	5.0	Right posterior	6.40	Mild	41	PFO	Serial echo follow-up
16	8.0/female	7.0	Right posterior near bifurcation	0.55	Moderate	64	N	Serial echo follow-up
17	12.0/female	8.9	Right-facing sinus	3.67	Severe	55	MVP	Serial echo follow-up
18	14.0/female	7.6	Right posterior near bifurcation	2.84	Mild	40	PDA	Serial echo follow-up
19	15.0/female	8.9	Right posterior	5.25	Moderate	34	N	Serial echo follow-up
20	21.0/female	10.0	Right-facing sinus	3.74	Moderate	67	MVP	Serial echo follow-up
21	29.0/male	14.0	Right posterior	4.15	Severe	60	N	Serial echo follow-up
22	46.0/male	16.0	Left posterior	2.52	Moderate	58	N	Serial echo follow-up
23	60.0/female	16.0	Posterior	4.67	Moderate	43	N	Serial echo follow-up
24	92.0/female	23.0	Left-facing sinus	−0.62	Mild	66	N	Echo follow-up
25	117.0/female	28.0	Left-facing sinus	1.43	Moderate	67	N	Echo follow-up
26	161.0/female	39.0	Right posterior	2.65	Moderate	69	N	Echo follow-up

ECMO: Extracorporeal membrane oxygenation; LCA: Left coronary artery; LVEF: Left ventricular ejection fraction; LVEDD: Left ventricular end-diastolic diameter; MVR: Mitral valve regurgitation; PA: Pulmonary artery; PFO: Patent foramen ovale; MVP: Mitral valve prolapse; ALCAPA: Anomalous left coronary artery from the pulmonary artery; CoA: Coarctation of the aorta; PDA: Patent ductus arteriosus; N: Without other concomitant anomaly.

deviation, whereas skewed continuous data were expressed as median (range). Categorical data were summarized as frequencies and percentages. Statistically significant differences were indicated when $P < 0.05$.

Results

From September 2008 to March 2017, 26 children diagnosed with ALCAPA underwent LCA re-implantation. The patients were diagnosed with ALCAPA at a median age of 4.5 months (range: 43 days – 13 years). The main clinical manifestations were respiratory tract infection, heart failure, dyspnea, feeding intolerance, and failure to thrive. The median age at operation was 4.9 months (range: 45 days – 13 years). Sixteen (61.5%) patients were <1 year old. The median weight at operation was 6.0 kg (range, 4.3–39.0 kg).

Early mortality was defined as death within 30 days of the operation. All other deaths were considered late mortality. The early mortality rate was 7.7% (2 of 26 patients) because of congestive cardiac failure and arrhythmia. The late mortality rate was 3.8% (1 of 26 patients, a girl who underwent surgery at 4 months of age and died 5 months after the operation because of persistent LV dysfunction).

All the other surviving patients (23 of 26 patients [88.4%]) received echocardiographic during follow-up (median follow-up of 32 months; range: 3 months to 8 years). Two infants (one aged 1.5 months and the other aged 3.0 months) required extracorporeal membrane oxygenation (ECMO) after the operation. One 1.5-month-old infant was operated in March 2017. Nineteen patients (73.1%) underwent serial postoperative echocardiography during follow-up (median follow-up of 40 months; range: 3 months to 8 years). Serial postoperative echocardiography was performed after the operation (on the 1st day, the 3rd day, the 7th day, the 14th day, the 1st month, the 3rd month, the 6th month, and so on until LV function was normal and then performed once every year).

Left ventricular function and size

Before repair, twenty patients (76.9%) presented with LV dysfunction. The median preoperative LVEF was 46% (range: 27–69%). Seven patients (26.9%) had a preoperative LVEF <40%. The mean *Z*-score for the preoperative LV end-diastolic diameter was 4.42 ± 2.09. Twenty-four patients (92.3%) presented with endocardial fibroelastosis on echocardiography. Aneurysm formation was present in one patient (3.8%).

Twenty-three patients received the echocardiography during follow-up. The mean LVEF after operation in these patients was 66.0 ± 7.0% (compared with a mean preoperative LVEF of 48.0 ± 12.9%; $P = 0.000$). The mean *Z*-score for the postoperative LV end-diastolic diameter was 1.28 ± 1.08 (compared with a mean preoperative *Z*-score of 4.18 ± 2.11, $P = 0.000$). The echocardiography studies demonstrated an improvement in LV function in all the surviving children. Serial postoperative echocardiograms were available for 19 patients. Five patients (26.3%) presented with normal LVEF before the operation. In the other 14 patients, LV function normalized at a median time of 5.3 months (range: 0.5–36.0 months). The *Z*-score for LV end-diastolic diameter also decreased within the same period. However, two patients who presented with severe myocardial dysfunction (LVEF was 34% and 38%, respectively) upon diagnosis still displayed abnormal features, such as echo-dense papillary muscles and endocardium, despite normal LVEF.

Degree of mitral regurgitation

MR was present in all patients before the operation: it was mild in 7 patients (26.9%), moderate in 14 patients (53.9%), and severe in 5 patients (19.2%). Two patients (7.7%) underwent mitral valve repair at the time of ALCAPA repair (both had mitral valve prolapse). After the operation, none of these patients required additional mitral valve repair. MR was reduced in all patients [Table 2]. At the most recent follow-up, 4 patients were free of MR and 15 patients had mild MR.

Patency of the left coronary artery

Since there was no sign of coronary obstruction in any of the surviving patients, no routine coronary angiography was performed after the operation. We used the parasternal aorta short-axis view to obtain the origin and course of the LCA with cross-sectional imaging. Color Doppler flow imaging was used to observe the distribution of blood flow, especially the LCA blood flow after the operation. All the surviving patients had patency of the proximal LCA that was confirmed by echocardiography at the most recent follow-up.

Complications

Supravalvar pulmonary stenosis and right pulmonary stenosis have been described as complications of the surgical approach. Six of the surviving patients (26.1%) showed supravalvar pulmonary stenosis and seven patients (30.4%) showed right pulmonary stenosis during the follow-up. The follow-up echocardiography showed a systolic infundibular dynamic gradient of 13.0–40.7 mmHg. None of the patients presented signs of aortic valve incompetence at the long-term echocardiography follow-up.

Discussion

Echocardiography is an important non-invasive auxiliary examination for diagnosing and functionally evaluating suspected congenital heart disease, including ALCAPA, in infants and children.[6,7] In addition, it serves as an important imaging tool for assessing outcomes after operation. After the ALCAPA operation, echocardiography can confirm the prograde flow from the aorta into the LCA. It can also follow the recovery of the LV function and the improvement of MR.

In many centers, direct re-implantation of the LCA into the aorta include coronary button transfer that had been proven successful and is considered the standard surgical strategy.[8-10] The operation is performed to establish a

Table 2: Surgical outcomes of ALCAPA by follow-up echocardiography

Patient number	Age (months)	Serial echo follow-up	Mitral valve repair	LV function normalized time (months)	Preoperation			Postoperation		
					LVEF (%)	*Z*-score of LVEDD	Degree of MR	LVEF (%)	*Z*-score of LVEDD	Degree of MR
1	1.5	Y	N	2.0	58	3.52	Moderate	60	0.59	Mild
2	1.7	Y	N	0.5	48	3.80	Mild	71	1.48	Free
3	2.0	Y	N	1.0	50	5.55	Mild	68	0.99	Mild
4	3.0	N	N	/	27	5.60	Moderate	66	0.21	Mild
5	3.2	Y	N	0.5	42	3.39	Mild	61	2.30	Free
6	3.5	Y	N	7.0	30	7.12	Severe	69	1.95	Moderate
7	4.0	Y	N	8.0	48	3.54	Moderate	71	−0.85	Free
8	4.2	Y	N	4.5	38	6.62	Severe	72	0.60	Mild
9	4.5	Y	N	5.5	38	7.70	Severe	71	1.90	Moderate
10	4.8	N	N	/	35	6.87	Mild	43	4.15	Mild
11	5.0	Y	N	13.0	41	5.21	Moderate	63	1.23	Moderate
12	5.5	Y	N	6.0	41	6.40	Mild	64	0.03	Mild
13	8.0	Y	N	/	64	0.55	Moderate	74	1.76	Free
14	12	Y	Y	16.0	55	3.67	Severe	65	1.64	Moderate
15	14	Y	N	5.0	40	2.84	Mild	63	1.83	Mild
16	15	Y	N	36.0	34	5.25	Moderate	62	1.76	Mild
17	21	Y	Y	/	67	3.74	Moderate	75	2.40	Mild
18	29	N	N	/	60	4.15	Severe	74	1.50	Moderate
19	46	N	N	/	58	2.57	Moderate	68	1.87	Mild
20	60	Y	N	3.0	43	4.67	Moderate	66	1.72	Mild
21	92	Y	N	/	66	−0.62	Mild	72	−0.62	Free
22	117	Y	N	/	67	1.43	Moderate	60	0.35	Mild
23	161	Y	N	/	69	2.65	Moderate	61	0.68	Mild

LVEF: Left ventricular ejection fraction; LVEDD: Left ventricular end-diastolic diameter; MR: Mitral regurgitation; LV: Left ventricular; ALCAPA: Anomalous left coronary artery from the pulmonary artery; Y: Yes; N: No; /: Not available.

dual coronary system. All patients had undergone LCA re-implantation to the aorta at our center. Our results confirmed the findings of other centers that building a dual coronary system with direct LCA re-implantation is the preferred method for managing ALCAPA.

The postoperative course was variable. Despite the establishment of a dual coronary system, some patients may experience extensive irreversible LV myocardial damage and present constant LV dysfunction. However, the surgical outcomes of most patients are encouraging. Naimo *et al*.[4] summarized the mortality from previous studies and concluded that early mortality in patients with ALCAPA was 0–16% in some centers; late mortality was rare, and survival rates of 86–100% at 10 years have been reported. In our research, the early mortality rate was 7.7%, and the late mortality rate was 3.8%.

Preoperative LV dysfunction and/or more severe preoperative MR were reported as incremental risk factors for postoperative mortality.[11] In some centers, earlier age might also have been related to mortality, probably because of inadequate coronary collateral development or more severe ventricular ischemia or dysfunction or both.[12] However, in our study, the preoperative LVEF, degree of preoperative MR, and age at operation were not seemed to be significant risk factors for mortality outcomes. Caspi *et al*.[13] reported that increased support with a positive inotropic agent and/or ECMO might be required in younger patients. We had a similar outcome, probably because those patients had less hibernating myocardium and less development of coronary collaterals than that of older patients.[13,14]

Mid- and long-term LV function and clinical status improved over time. Some patients, especially younger ones and those with severe LV dysfunction, might require a period of LV support to allow the recovery of both stunned and hibernating myocardia. Serial postoperative echocardiography during follow-up showed complete recovery of LV function in all the surviving patients in our study. In patients whose preoperative LVEF <40%, LV function normalized at a median time of 6.3 months (range: 4.5 to 36.0 months). Our study demonstrated that, in 78.6% of patients (11 out of 14 patients), the normalization of LVEF and LV functional factors occurred within one year after the operation. LVEF and LV dilatation improved over the ensuing 2–3 months, probably reflecting the recruitment of hibernating or chronically ischemic myocardium. In patients whose preoperative LVEF ≥40%, the median normalized time was 4.0 months (range: 0.5 - 16.0 months). It appeared that patients with lower preoperative LVEF required more time for normalization. However, the number of patients in our study was small, and consequently, we could not perform statistical comparisons. Patients whose preoperative LVEF was normal tended to have normal LV function quickly after the operation, possibly because they had developed a rich

collateral system between two coronary arteries that could ameliorate myocardial ischemia. However, they also needed time to achieve a normalized LV end-diastolic diameter. Patients who presented with severe myocardial dysfunction before the operation still displayed abnormal features, such as echo-dense papillary muscles or endocardium, in the most recent echocardiography follow-up. However, standard echocardiography might be less than perfect in some ways, such as detecting scars and perfusion deficits in the LV. In those patients, especially older children, lifelong surveillance with MRI and myocardial perfusion imaging might be needed to detect and evaluate dysfunction.[14]

Due to LV dilatation and ischemic cardiomyopathy, MR is considered a coexistent manifestation in most patients with ALCAPA.[15] In some patients, MR might be the only indication suggesting ALCAPA. Whether to repair the mitral valve at the same time as the LCA re-implantation remains controversial. Several studies have reported that simultaneous mitral valve repair had no effect on the normalization of LV function or other surgical outcomes, although the degree of MR might improve after the operation. These studies did not advocate addressing the mitral valve at the same time as the ALCAPA repair, regardless of MR severity.[14-17] Other researchers have suggested that mitral valve repair is needed only when the valve is structurally defective.[18] In our study, MR was present in all patients before the operation. Nineteen patients had preoperative moderate or severe MR, and only two patients underwent mitral valve repair during the ALCAPA repair because of the mitral valve structural problem (both patients had mitral valve prolapse). Echocardiography is a vital tool for evaluating the degree of MR. With follow-up echocardiography, especially serial postoperative follow-up echocardiography, we could observe the changes in the MR after the operation. In the two patients with a structurally defective mitral valve, MR was reduced after the operation. During our follow-up period (4–5 years), these patients did not need further mitral valve operation. In other patients, including three with severe MR, the degree of MR decreased as the LV function improved. MR tended to improve postoperatively once a dual coronary system was restored. This could be the result of the decrease in mitral annular diameter with the reduction in LV dimensions and improved perfusion of the myocardium (particularly the papillary muscle). No patient in our series required late mitral valve replacement. In the majority of patients with ALCAPA seen at our center, both LV function and MR normalized over time. Improvements in MR suggested ischemic recovery, which might lag behind the normalization of LV function. Therefore, intervention in patients without structurally defective mitral valve did not seem necessary.

The high rate of late LCA patency after direct implantation was proven.[19] Echocardiography could determine the patency of the proximal LCA. We used the parasternal aorta short-axis view with cross-sectional imaging to obtain the origin and course of the LCA and the blood flow after the operation. However, echocardiography had some difficulty in displaying the distal coronary artery. Therefore, we also needed to focus on other features, such as LV function and MR. Postoperative coronary stenosis should be suspected in a patient with persistent LV dysfunction. Worsening MR also reflected the patency of the LCA. Coronary stenosis might also exist when MR recurs or persists for a long time. Cardiac catheterization should be performed to assess the patency of the LCA before performing additional mitral valve surgery.[11] Standard electrocardiography and MRI were also suggestive. If serious coronary stenosis exists, patch angioplasty should be performed.[16,20] No patient at our center required reoperation for coronary stenosis. All surviving patients were asymptomatic after the operation. Standard electrocardiography revealed no arrhythmias or ischemic change, such as T-wave change, in any of the investigated patients. No routine coronary angiography was performed. Postoperative echocardiograms demonstrated a patent LCA in all patients. All surviving patients had patency of the proximal LCA confirmed with echocardiography at the most recent follow-up.

Supravalvular pulmonary stenosis is a late complication of surgery for anomalous coronary origin.[21] Supravalvar pulmonary stenosis and right pulmonary artery stenosis had been described as a result of pulmonary artery reconstruction. In our research, no patient required an additional operation because of this complication.

Since the incidence rate of ALCAPA is low and our study was a single-center study, the number of patients and outcomes were small. For this reason, statistical analysis was limited (statistical comparisons and a descriptive study could not be performed). This study also had the limitations of a retrospective study. Additional studies are necessary in the future.

In conclusion, this study provides insight into the correlation between echocardiography changes (such as LV function, MR, and surgical complications) and the surgical outcomes of ALCAPA over time. Our study appeared to be consistent with previous studies in terms of mortality, recovery of the LV function, and improvement of MR. Coronary re-implantation was effective for rebuilding a dual coronary system in patients with ALCAPA and resulted in the progressive improvement of LV function. MR tended to improve without structural defects of the mitral valve. Echocardiography is valuable for evaluating the therapeutic effect of coronary re-implantation.

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Conflicts of interest

There are no conflicts of interest.

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