A Single-Center Retrospective Study of Patients with ALCAPA

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ABSTRACT

Introduction: Anomalous left coronary artery from the pulmonary artery (ALCAPA) is a rare but fatal disease. Untreated cases have a first-year mortality rate of 90%. We aimed to evaluate the early outcomes of patients who were operated on for ALCAPA in our clinic.

Patients and Methods: We retrospectively reviewed the cases of seven patients who were operated on in our clinic for ALCAPA between 2013 and 2019. Preoperative, early postoperative, and first year echocardiography results were compared.

Results: Five patients (71.4%) underwent reimplantation and two patients (28.6%) underwent Takeuchi repair. The median age was 25 months and 71.4% (n= 5) of the patients were aged ≤1 year. In preoperative echocardiograms, mean ejection fraction (EF) was 32.1 ± 4.9% and mean preoperative MR grade was 2.1 ± 0.7. Two patients with severe MR (grade 3) underwent simultaneous mitral annuloplasty. The mean EF % significantly increased (p= 0.023) and the mean MR grade significantly decreased (p= 0.039, p< 0.05) in the early postoperative period. This finding was not statistically associated with surgical technique or age. The mortality rate was 14.3% (n= 1). The patient who died had severe preoperative LV dysfunction and MR, which did not improve after surgical intervention.

Conclusion: Early improvement in LV function and MR grade after ALCAPA repair is crucial for survival regardless of age. Moderate or mild functional MR may spontaneously improve after the surgical correction of LV dysfunction. Simultaneous mitral valve intervention is needed in cases of severe MR and patients aged ≥1 year.

Key Words: Left coronary artery; pulmonary artery; coronary artery reimplantation

ALCAPA Tanılı Hastalarda Tek Merkezli Retrospektif Çalışma

ÖZET

Giriş: Sol koroner arterin pulmoner arterden anormal orijini (ALCAPA), konjenital kalp hastalıklarının %0.5'ini oluşturan nadir ama fatal seyreden bir hastalıktır. Tedavi edilmeyen olgularda ilk yılda mortalite %90'dır. Kliniğimizde ALCAPA tanısıyla opere edilen hastaların erken dönem sonuçlarını değerlendirmeyi amaçladık.

Hastalar ve Yöntem: Kliniğimizde 2013-2019 yılları arasında ALCAPA tanısı ile opere edilen yedi hasta retrospektif olarak incelendi. Hastaların preoperative ve postoperative bulguları, özellikle LV ve mitral kapak fonksiyonu üzerinde duruldu.

Bulgular: Hastaların %71.4'üne (n= 5) reimplantasyon prosedürü ve %28.6'sına (n= 2) Takeuchi prosedürü uygulanmıştı. Ortalama yaş 25 ay olup, %71.4 (n= 5)'i ≤1 yaş idi. Hastaların preoperatif ejeksiyon fraksiyonu (EF) %32.1 ± 4.9 ve preoperatif mitral yetmezlik (MR) derecesi ortalama 2.1 ± 0.7'ydi. Ciddi MR (3. seviye) olan iki hastaya eş zamanlı mitral anuloplasti yapıldı. Postoperative erken dönem EF % değerlerinde artış (p= 0.023) ve MR derecelerinde azalma görüldü (p= 0.039, p< 0.05). Hastaların yaşlarıyla preoperative ve postoperative bulguları arasında anlamlı farklılık saptanmadı. Mortalite oranı %14.3 (n= 1) idi. Preoperatif ciddi sol ventrikül (LV) disfonksiyonu ve MR olan hastanın postoperative EF ve MR derecesinde değişiklik saptanmamıştır.

Sonuç: ALCAPA tamiri sonrası LV disfonksiyonu ve MR derecesi yaştan bağımsız olarak hayatidir. Orta ve daha az şiddette olan preoperative fonksiyonel MR, postoperative dönemde LV fonksiyonlarının düzelmesiyle azalabilir. Ciddi MR ve >1 yaş olan hastalarda eş zamanlı mitral kapak müdahelesi yapılmalıdır.

Anahtar Kelimeler: Sol koroner arter; pulmoner arter; koroner arter reimplantasyonu

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INTRODUCTION

Anomalous origin of the left coronary artery from the pulmonary artery or ALCAPA, was first described by Bland, White and Garland in 1933 and is accordingly also known as Bland-White-Garland syndrome[1]. It is a rare congenital heart disease and affects one in 300.000 live births[2]. The anomalous left main coronary artery typically originates from the left or posterior sinus of the pulmonary artery and proceeds to branch normally[3,4]. In the setting of inadequate coronary collateralization after birth, severe left ventricular (LV) myocardial ischemia and dysfunction will occur. Secondary mitral regurgitation (MR) of varying degree is present in most cases[5]. Its treatment requires surgery and various techniques have been developed over time. In this study, we share the early outcomes of patients who underwent ALCAPA repair in our clinic.

PATIENTS and METHODS

We retrospectively reviewed the cases of patients who underwent ALCAPA repair in our clinic between 2014 and 2019. The study was granted approval by the institutional ethics committee (Date 12.01.2021, Number 2021/1/423). The patients were compared in terms of demographic characteristics, surgical methods, and echocardiography findings. LV function was assessed with M-mode echocardiography pre- and postoperatively and one year after the intervention. LV dysfunction was defined as an ejection fraction (EF) below 50%. The change between pre- and early postoperative EF % was defined as ΔEF_1 (preoperative-early postoperative) and the change between early and one-year outcomes was defined as ΔEF_2 (preoperative-early postoperative first year). Mitral valve insufficiency (MR) was evaluated according to conventional guidelines as grade 0 (no MR), grade 1 (mild MR), grade 2 (moderate MR), grade 3 (severe MR), or grade 4 (most severe MR)[6].

Statistical Analysis

Data were analyzed using SPSS 26.0 (IBM Corp., Armonk, NY, USA). For univariate analysis, the Shapiro-Wilk Francia test was used to assess the normality of distribution. The Wilcoxon signed rank test was used to compare repeated measurements of dependent quantitative variables. The Friedman two-way test was used with Monte Carlo simulation in the comparison of repeated measurements of multiple dependent variables. Stepwise step-down comparisons were performed for multiple comparisons. In the tables, quantitative variables are presented as mean (standard deviation) or median (minimum/maximum), and categorical variables are presented as n (%). The variables were analyzed at the 95% confidence level and a p-value of less than 0.05 was considered significant.

RESULTS

Demographic findings are summarized in Table 1. The median age was 25 months (range: three months to 15 years) and 71.4% (n= 5) of the patients were aged ≤1 year. The average follow-up time was 23.5 ± 13.7 months (range: 0-50 months). Five patients (71.4%) underwent reimplantation and two patients (28.6%) underwent Takeuchi repair.

The mean preoperative EF % was 32.1 ± 4.9, the mean early postoperative EF % was 50.0 ± 11.5, and, for surviving patients, the mean one-year EF % was 62.5 ± 2.7. The early postoperative increase in EF % was statistically significant. The mean preoperative MR grade was 2.1 ± 0.7 and the mean postoperative MR grade was 1.0 ± 0.6 (Table 2). Two patients (28.6%) with grade 3 MR aged six and 15 years, respectively, underwent simultaneous mitral annuloplasty. Mitral valve intervention was not performed for patients aged ≤1 year or patients with MR grade of ≤2. The mean MR grade significantly decreased after treatment. Preoperative, early postoperative, and one-year echocardiography results were not significantly associated with age. Age was only significantly associated with the duration of postoperative intubation (Table 3).

Preoperative and postoperative MR grades were significantly associated with preoperative EF but not with early postoperative or one-year EF. Cardiopulmonary bypass time directly affected early preoperative EF, and the change in MR grade was associated with the duration of intubation (Table 4).

The mortality rate was 14.3% (n= 1). The patient who died was five months old and had undergone Takeuchi repair. This patient had a preoperative EF of 25%, i.e. severe LV dysfunction. EF and MR grade did not improve in the early postoperative period and the patient required extracorporeal membrane oxygenation (ECMO).

DISCUSSION

Surgical correction is the gold standard of treatment for ALCAPA repair and several techniques have been described in the literature[6,7]. There is no consensus on the best surgical technique for treating ALCAPA[8]. In our clinic, reimplantation is the preferred method for the treatment of ALCAPA, decided perioperatively based on the origin of the anomalous coronary artery. If ALCAPA arises from the posterior facing sinus of the pulmonary artery, the classical reimplantation procedure is performed. ALCAPA is transected at its origin from the pulmonary artery. After it is mobilized from the surrounding tissue, it is anastomosed, taking care not to disrupt the coronary flow to the aorta (Figure 1). In our study, five patients (71.4%) underwent reimplantation, four of whom had a left coronary artery arising from the posterior side of the pulmonary artery and one from

Table 1. Patient demographic data, preoperative and postoperative findings

Patient Number	1	2	3	4	5	6	7
Gender	Female	Male	Female	Female	Male	Female	Female
Age	15 year	7 month	5 month	5 month	6 year	1 year	3 month
Weight (kg)	42	6	5	4	20	8	3
Abnormal coronary orginate	LPA	PFS	PFS	NFS	PFS	NFS	PFS
Misdiagnosis	C.AVF	-	-	DKMP	-	-	-
Surgery procedure	R	R	R	T	R	T	R
EF %							
Preoperative	40	30	35	**25**	30	35	30
Early postoperative	55	50	60	**25**	50	55	55
First year	60	65	60	0	65	60	65
EF Δ 1 (preoperative-early postoperative)	15	20	25	0	20	20	25
EF Δ 2 (preoperative-first year)	20	35	25	0	35	25	35
MR grade							
Preoperative	3	1	2	2	3	2	2
Postoperative	0	1	1	**2**	1	1	1
X clamp time	106	120	81	**155**	128	145	153
CPB time	130	152	100	**180**	145	167	120
Intubation time (hour)	10	36	30	192	7	12	45
ICU time (day)	2	5	2	8	3	6	7
Length of hospital stay (day)	8	13	7	15	7	12	15
Follow-up time (months)	50	26	15	0	17	20	13
Mitral annuloplasty	+	-	-	-	+	-	-
Re-operation	-	-	-	-	-	-	-
Prolonged ventilation	-	-	-	+	-	-	+
ECMO	-	-	-	+	-	-	-

LPA: Left pulmonary artery, PFS: Posterior facing sinus, NFS: Nonfacing sinus c.avf: coronary arterio-venous fistula, DKMP: Dilated cardiomyopathy, R: Reimplantation procedure, T: Takeuchi procedure, EF: Ejection fraction, MR: Mitral regurgitation, CPB: Cardiopulmonary bypass, ICU: Intensive care unit, ECMO: Extracorporeal membran oxygenation.

the left pulmonary artery. In our clinic, if ALCAPA originates from a non-facing sinus, the Takeuchi procedure is preferred. In the Takeuchi procedure, after creating an aortopulmonary window, we do not use pulmonary flaps during tunneling, unlike the classical procedure. Instead, the tunnel is created by anastomosing the posterior face with the pulmonary artery and the anterior face with an autologous pericardial patch. Again, the main pulmonary artery is reconstructed with an autologous pericardial graft in every patient to alleviate the risk of postoperative PS (Figure 2). In our study, Takeuchi repair was performed for 28.6% of patients. Neither of those patients developed surgical complications or required reoperation, but one patient who underwent Takeuchi repair died.

Standard echocardiographic data have confirmed that systodiastolic LV function recovers after successful surgery in most patients, but residual myocardial fibroelastosis is relatively common, although well tolerated[9]. Although the causes of functional recovery are only partially understood, some authors have associated it with hibernating myocardium[10,11]. Another theory is that healthy myocytes reduce scar tissue and proliferation[10,12]. Latus et al. argued that despite the improved LV function after successful reimplantation, scar tissue is visible on MRI and the possibility of permanent or recurrent myocardial damage and subclinical ischemia still persists[13,14]. Similarly, Secinaro et al. and Fratz et al. reported myocardial scarring in 71% of patients after repair despite normal LV function

Table 2. Comparisons of ejection fraction (EF %) and mitral regurgitation (MR) grade

			Median (min/max)	p
EF %				**0.015[f]**
	Preoperative	A	30 (25/40)[C]	P (A-B)= 0.247
	Early postoperative	B	55 (25/60)	**P (A-C)= 0.023**
	First year	C	60 (0/65)	P (B-C)= 0.999
MR grade				**0.039[w]**
	Preoperative		2 (1/3)	
	Postoperative		1 (0/2)	

f Friedman Test (monte carlo); Post hoc test: Stepwise step-down comparisons,
w Wilcoxon Signed Ranks Test (monte carlo).
A Expresses significance according to preoperative EF.
B Expresses significance according to early postoperative EF.
C Expresses significance according to 1st year EF.
EF: Ejection fraction, MR: Mitral regurgitation.

Table 3. Correlations with Age

		r	p
EF % Preoperative	Age (month)	0.519	0.232
EF % Early postoperative	Age (month)	-0.076	0.872
EF % 1st year	Age (month)	0.000	0.999
EF Δ1	Age (month)	-0.481	0.274
EF Δ2	Age (month)	-0.123	0.793
MR grade preoperative	Age (month)	0.603	0.152
MR grade postoperative	Age (month)	-0.607	0.149
MR grade Δ (preoperative-postoperative)	Age (month)	-0.633	0.127
Intubation time (hour)	Age (month)	-0.847	**0.016**
ICU stay (day)	Age (month)	-0.555	0.196
Hospital stay (day)	Age (month)	-0.569	0.183

Spearman's rho test, r: Correlation coefficient.
EF: Ejection fraction, EF Δ1: Preoperative-early postoperative, EF Δ2: Preoperative-first year, MR: Mitral regurgitation, MR grade Δ: Preoperative-postoperative, ICU: Intensive care unit.

but did not associate this finding with LV size or function[10,15].

Kudumula et al. reported normal LV function in 88% of infants and children with ALCAPA in late follow-up[16]. Other studies demonstrated significant improvement in LV function. In 2017, Zhang et al. demonstrated satisfactory improvement in heart function even in patients with severe ventricular dysfunction and myocardial infarction[17]. In 2020, the another study suggested that LV function temporarily decreased in the early postoperative period and returned to normal after 14 days[18].

The restoration of correct anatomy allows the rapid recovery of LV function at one year after surgery[11,19,20]. In a study conducted in our country, it was suggested that early diagnosis positively affects the success of treatment and that coronary artery origins should be evaluated in terms of ALCAPA, especially in patients with dilated cardiomyopathy[21].

The literature, however, contains insufficient data on the effect of patient age on the improvement of LV function after ALCAPA repair[22]. Some studies have suggested that early surgery accelerates the recovery of ventricular dysfunction, which was confirmed by Stern et al., who demonstrated perfusion defects with thallium-201 imaging[23].

In our study, EF % values significantly increased in the early postoperative period, in accordance with the literature (p= 0.023). ΔEF_1 was 17.9 ± 8.6 and ΔEF_2 was 25.0 ± 12.6,

Table 4. Correlations with ejection fraction (EF %)

		r	p
MR grade preoperative	EF % preoperative	-0.660	**0.010**
MR grade postoperative	EF % preoperative	-0.840	**0.018**
MR grade Δ	EF % preoperative	-0.667	0.102
MR grade preoperative	EF % early postoperative	0.094	0.841
MR grade postoperative	EF % early postoperative	-0.560	0.191
MR grade Δ	EF % early postoperative	-0.441	0.322
MR grade preoperative	EF % 1st year	-0.086	0.854
MR grade postoperative	EF % 1st year	-0.289	0.530
MR grade Δ	EF % 1st year	-0.141	0.762
MR grade preoperative	EF Δ1	-0.250	0.588
MR grade postoperative	EF Δ1	-0.140	0.765
MR grade Δ	EF Δ1	-0.059	0.900
Follow-up time (month)	EF Δ1	-0.168	0.718
MR grade preoperative	EF Δ2	-0.209	0.653
MR grade postoperative	EF Δ2	-0.140	0.765
MR grade Δ	EF Δ2	-0.020	0.967

Spearman's rho test, r: Correlation coefficient.
EF: Ejection fraction, EF Δ1: Preoperative-early postoperative, EF Δ2: Preoperative-first year, MR: Mitral regurgitation, MR grade Δ: Preoperative-postoperative.

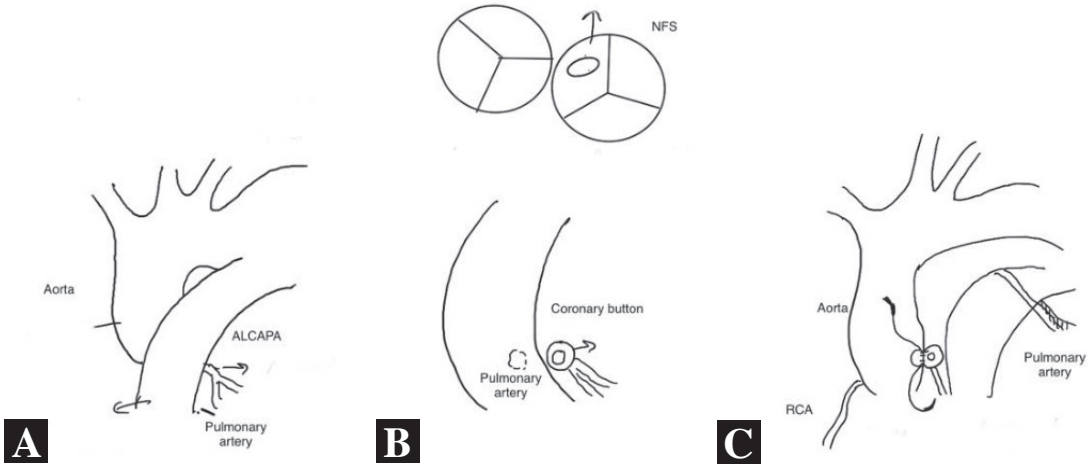

Figure 1. Reimplantation procedure.
A. Assessment of ALCAPA origin, **B.** Preparation of ALCAPA in the form of coronary button, **C.** Direct reimplantation of ALCAPA.
NFS: Non facing sinus, ALCAPA: Anomalous origin of the left coronary artery the pulmonary artery, RCA: Right coronary artery.

and LV dysfunction improved in the early postoperative period (i.e. the first two weeks after surgery) and then plateaued, with minimal improvement thereafter. There was no correlation between age and the change in EF.

One major factor that influences the outcome of ALCAPA repair is MR severity[24]. The etiology involves the ischemic dysfunction of papillary muscles and LV enlargement resulting in mitral annular enlargement[9,17,24]. The timing of mitral valve repair during ALCAPA remains controversial. Indeed, especially in infants, MR may gradually decrease or remain stable in patients with mild to moderate preoperative MR without requiring mitral valve repair or replacement[25]. Several

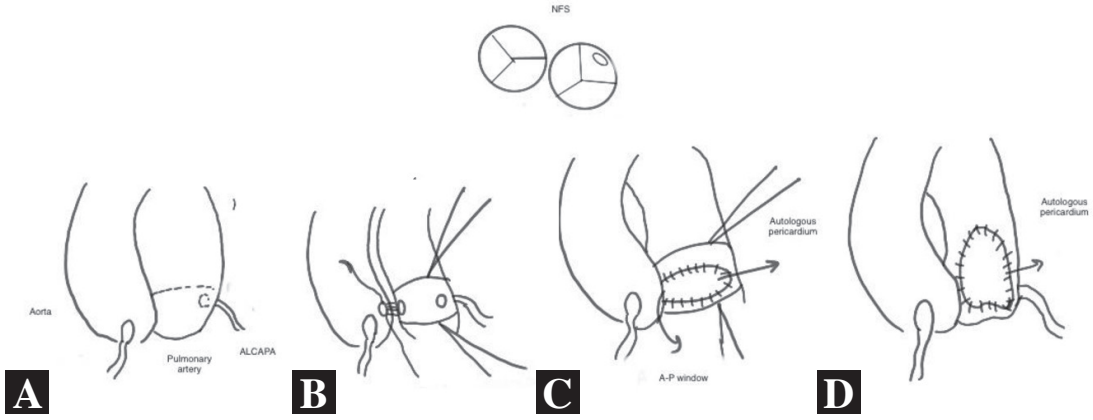

Figure 2. Takeuchi procedure.

A. Pulmonary incision, **B.** A-P window creation, **C.** Baffle creation with autologous pericardium, **D.** Closure of pulmonary artery defect with autologous pericardium.

NFS: Non facing sinus, ALCAPA: Anomalous origin of the left coronary artery the pulmonary artery, A-P window: Aorta-pulmonary arter window.

studies have reported that simultaneous mitral valve repair had no effect on the normalization of LV function or other surgical outcomes[20,25].

Some researchers have suggested that simultaneous mitral annuloplasty should be performed for all patients undergoing ALCAPA repair, regardless of MR grade[26,27], as it may improve early postoperative cardiac output and reduce operative mortality[28]. Neumann et al. recommended simultaneous surgery for patients who preoperatively have moderate or severe MR, especially if left ventricular ejection fraction (LVEF) is normal upon admission. In addition, postoperatively, MR improves much more rapidly in younger patients, as is the case with LVEF[29].

Since annuloplasty does not accommodate growth, it cannot be applied to infants and young children and needs to be substituted by the surgical repair of the chordae and papillary muscles. Due to being time-consuming and technically demanding, mitral valve repair during initial surgery can increase ischemic time, which can be detrimental to an already compromised myocardium.

In our study, age was not associated with pre- or postoperative findings. Two patients (28.6%) with grade 3 MR, aged six and 15 years, respectively, underwent simultaneous mitral annuloplasty. Patients younger than one year of age and patients with moderate or mild MR did not undergo mitral valve intervention, and with improvement in LV dysfunction, MR grades decreased significantly in the postoperative period (p= 0.039). In our clinic, we perform mitral valve intervention for patients aged over one year, patients with severe MR, and patients with organic MR pathologies on preoperative echocardiography scans.

Mechanical support, including ECMO and left ventricular assist devices, have yielded promising results, particularly in children with severe myocardial ischemia and ventricular dysfunction[29]. Different centers adopt different strategies for using mechanical support devices[8]. Reduced EF and severe LV dilatation were reported to predict mortality in some studies[30]. In other studies, they were associated with intraoperative myocardial protection[9].

The literature reports operative mortality rates between 0% and 23%[3,24]. Preoperative LV dysfunction and/or more severe preoperative MR are risk factors for increased postoperative mortality[30]. A younger age was associated with mortality in some centers[30]. Lange et al. suggested that these risk factors were significant for mortality, while Gao et al. indicated that they were not[22,31]. Similarly, Schwartz et al. reported that preoperative MR did not predict mortality whereas Caspi et al. reported that a younger age was not a risk factor for mortality but was associated with an increased need for positive inotropic and/or ECMO support. It is also associated with reduced hibernating myocardium and collateralization[31,32].

In our study, the mortality rate was 14.3% (n= 1). This patient had the lowest preoperative EF % in the patient series and also had grade 2 mitral regurgitation. LV dysfunction did not improve in the early postoperative period and the patient required ECMO. Echocardiography prior to the Takeuchi procedure revealed no problems with tunneling or coronary blood flow. All patients were operated on under moderate hypothermia and the same cardiological principles; therefore, mortality was not associated with myocardial protection.

CONCLUSION

Surgery should be performed early for patients diagnosed with ALCAPA, regardless of symptoms and age. Due to achieving a dual coronary system, reimplantation should be the treatment of choice. If it is not suitable, the Takeuchi procedure can be performed. Severe preoperative LV dysfunction and postoperative persistent LV dysfunction may predict mortality, although this finding is limited by our small sample size. Improved LV function may be sufficient to correct functional MR. Simultaneous mitral valve intervention may be beneficial in patients with severe MR.

Ethics Committee Approval: The study protocol was approved by the Kartal Koşuyolu High Specialization Training and Research Hospital Ethics Committee. The study was conducted in accordance with the principles of the Declaration of Helsinki (Decision no: 2021/1/423 Date: 12.01.2021).

Informed Consent: Informed consent was obtained.

Peer-review: Externally peer-reviewed.

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