Surgical Intervention for Anomalous Origin of Left Coronary Artery From the Pulmonary Artery in Children: A Long-Term Follow-Up

Phillip S. Naimo, MD, Tyson A. Fricke, MBBS, Yves d’Udekem, MD, PhD, Andrew D. Cochrane, MBBS, Andrew Bullock, MBBS, Terry Robertson, MBBS, Christian P. Brizard, MD, and Igor E. Konstantinov, MD, PhD

Department of Cardiothoracic Surgery, Royal Children’s Hospital, Melbourne; Department of Paediatrics, University of Melbourne, Melbourne; Murdoch Children’s Research Institute, Melbourne; Department of Cardiothoracic Surgery, Monash Medical Centre, Melbourne; Department of Cardiology, Princess Margaret Hospital for Children, Perth; and Department of Cardiology, Women’s and Children’s Hospital, Adelaide, Australia

Background. Anomalous left coronary artery from the pulmonary artery (ALCAPA) is a rare congenital heart defect with limited data on long-term outcomes after surgical intervention.

Methods. We conducted a retrospective review of all children (N = 42) who underwent surgical repair of ALCAPA between 1980 and 2014 at the Royal Children’s Hospital, Melbourne.

Results. Twenty-nine (69% [29 of 42]) patients underwent coronary reimplantation, 12 (29% [12 of 42]) had intrapulmonary baffle (Takeuchi) repair, and 1 (2% [1 of 42]) patient had ligation of the anomalous coronary artery. Nine (21%, 9 of 42) patients had concomitant mitral valve (MV) repair at the time of ALCAPA repair. A left ventricular assist device (LVAD) was used in 36% (15 of 42) of patients. Early mortality was 2.4% (1 of 42 patients). Median follow-up was 14 years (mean, 13 years; range, 4 months–31 years). There were no late deaths. Survival was 98% at 20 years. Freedom from reoperation was 81%, 81%, and 76% at 5, 10, and 20 years after operation, respectively. Eight patients underwent late MV repair or replacement at a median of 3 years (mean, 8 years; range, 2 months–25 years) after operation. Freedom from late MV repair or replacement was 86% at 5 and 10 years and 81% at 20 years after operation. Eleven (26% [11 of 42]) patients had severe mitral regurgitation (MR) preoperatively. Of those 11 patients, 5 (45% [5 of 11]) had concomitant MV repair at the time of ALCAPA repair, 3 (27% [3 of 11]) had late MV repair or replacement, and the remaining 3 (27% [3 of 11]) patients had mild MR at last follow-up. Thirty-six (90% [36 of 41]) patients had normal left ventricular function and 4 (10% [4 of 41]) patients had mildly reduced left ventricular (LV) function at last follow-up.

Conclusions. ALCAPA can be operated on with good outcomes. Persistent MR and a moderate rate of late MV repair warrants close follow-up.

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Address correspondence to Dr Igor E. Konstantinov, Royal Children’s Hospital, Flemington Rd, Parkville, VIC 3029, Australia; email: igor.konstantinov@rch.org.au.

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A nomalous left coronary artery from the pulmonary artery (ALCAPA) is a rare congenital anomaly, which if left unrepaired has a mortality rate up to 90% [1]. Left ventricular (LV) dysfunction and ischemic mitral regurgitation (MR) secondary to mitral annular dilatation and ischemic papillary muscle dysfunction contributes to the morbidity and mortality in this condition.

Several surgical techniques have been described for repair of ALCAPA, including ligation of the anomalous artery [2], bypass grafting [3], intrapulmonary artery baffle or Takeuchi repair [4], and coronary reimplantation to the aorta [5]. However, the decision to repair the mitral valve (MV) at the time of operation is controversial. After revascularization of the anterolateral wall of the left ventricle, the MV may regain reasonable function, despite severe preoperative MR.

Good early surgical outcomes of ALCAPA repair have been described [6–11]. We have previously reported on midterm outcomes of ALCAPA repair in a smaller group of patients [6]. There are few single-institution studies on the long-term outcomes of patients with ALCAPA, including outcomes related to the MV. Therefore we sought to review the surgical management of ALCAPA repair at our institution and to evaluate the associated MV disease, its management, and long-term outcomes.

Patients and Methods

Patients
The Human Research Ethics Committee at the Royal Children’s Hospital approved the study. Between 1980 and 2014, 42 children underwent repair of ALCAPA.
at the Royal Children’s Hospital. Data were obtained retrospectively by review of medical records from initial admission until last cardiology follow-up.

Definitions
Early mortality was defined as death occurring within 30 days of operation or before hospital discharge. All other deaths were considered late. Severity of MR was graded using conventional guidelines [12].

Data Analysis
Data were analyzed using Stata, version 12 (StataCorp LP, College Station, TX). Descriptive statistics for continuous data are expressed as mean ± standard deviations (range), whereas skewed continuous data are expressed as median (range). Categorical data are summarized as frequencies and percentages. Kaplan-Meier actuarial survival curves were used to analyze and plot time-related end points. Statistical significance was set at \( p < 0.05 \).

Results
From February 1980 to March 2014, 42 children underwent repair of ALCAPA at the Royal Children’s Hospital. Preoperative patient characteristics are summarized in Table 1. Median age at operation was 140 days (mean, 276 days; range, 49 days–5 years). There were 34 (81% [34 of 42]) patients less than 1 year of age. Median weight at operation was 5.7 kg (mean, 6.7 kg; range, 2.3–23 kg).

Repair of ALCAPA was done by reimplantation of the anomalous artery in 29 (69% [29 of 42]) patients, an intrapulmonary baffle (Takeuchi repair) in 12 (29% [12 of 42]) patients (Fig 1), and ligation of an anomalous left circumflex artery arising from the pulmonary artery in 1 (2% [1 of 42]) patient.

Nine (21%, 9 of 42) patients had concomitant MV repair at the time of the initial operation. The median age of patients who underwent concomitant MV repair was 147 days (range, 74 days–1.8 years) compared with 141 days (range, 78 days–5 years) in those who did not undergo such repair. There was no significant difference in age between those who had concomitant MV repair and those who did not (\( p = 0.87 \)). Mean cardiopulmonary bypass (CPB) time in patients who had concomitant MV repair was 184 ± 50 minutes compared with 137 ± 79 minutes in patients who did not have concomitant MV repairs (\( p = 0.09 \)). Mean aortic cross-clamp time in patients who had concomitant MV repair was 112 ± 22 minutes compared with 70 ± 39 minutes in patients who did not have concomitant MV repair (\( p = 0.006 \)). Of the concomitant MV repairs, 8 (89% [8 of 9]) were undertaken in patients who had reimplantation of the anomalous artery, and 1 (11% [1 of 9]) was undertaken in a patient who had a Takeuchi repair.

Additional concomitant repair occurred in 1 patient (2% [1 of 42]). This patient presented with incipient LV rupture through a transmural anterior infarction, which was resected and reconstructed [13]. At the completion of the operation, 15 patients (36% [15 of 42]) required a LV assist device (LVAD). This was a centrifugal pump with left atrial (LA) and aortic cannulation through a midline sternotomy and an open chest. Twelve of the 15 patients who required an LVAD were noted to have a significant rise in LA pressure and a reduction in mean arterial pressure after being weaned from CPB, which prompted the use of an LVAD. The remaining 3 patients received LVADs electively. There was no relationship between the use of LVADs and the time of aortic cross-clamping (LVAD, 95 ± 40 minutes versus no LVAD, 79 ± 45 minutes; \( p = 0.35 \)). The LVAD was removed at a mean of 4 ± 2 days (range, 2–8 days) after the operation. One patient was placed on extracorporeal membrane

![Table 1. Preoperative Patient Characteristics (n = 42)](image-url)
oxygenation 1 day after ALCAPA repair because of cardia
crrest and respiratory failure. She remained on extracorporeal membrane oxygenation for 1 day. She re-

Mortality

Early mortality was 2.4% (1 of 42 patients). In 2008, an 11-month-old girl weighing 6.5 kg presented with congestive cardiac failure and was found to have ALCAPA with mild MR and severe LV dysfunction. She underwent repair of ALCAPA through reimplantation. LV function remained poor when she was weaned from CPB and she received an LVAD. Four days postoperatively she had a cerebral infarction secondary to thromboembolism in the LVAD pump and died.

There were no late deaths. Overall survival was 98% ± 2% (95% confidence interval [CI], 86–100) at 5, 10, and 20 years.
Management of the Mitral Valve

Preoperatively, 13 (31% [13 of 42]) patients had mild MR, 18 (43% [18 of 42]) patients had moderate MR, and 11 (26% [11 of 42]) patients had severe MR. MV outcomes are shown in Figures 2A and 2B.

Concomitant MV repair was undertaken in 9 (21% [9 of 42]) patients—5 with severe MR and 4 with moderate MR. Six patients underwent suture annuloplasty, 2 patients underwent plication of part of the mitral valve, and 1 patient underwent ring annuloplasty. Two of these patients required additional MV repair at 70 days and 4.1 years, respectively. One patient has undergone 2 redo MV repairs because of persisting MR. Freedom from MV reoperation for those patients who underwent concomitant MV repair was 71% ± 18% (95% CI, 23–92) at 10 years (Fig 3).

An additional 6 patients, who did not have concomitant MV repair, underwent 7 late MV operations at a median of 3 years (range, 11 months–25 years) after initial ALCAPA repair because of persisting severe MR (n = 3) or MR worsening to a severe degree (n = 3) after ALCAPA repair. This consisted of MV repair in 4 patients and MV replacement in 2 patients. One patient has undergone 2 MV replacements at 1.5 years and 22 years after initial ALCAPA repair. Freedom from late MV repair or replacement in patients who did not undergo concomitant MV repair was 86% ± 6% (95% CI, 71–94) at 5 and 10 years and 81% ± 8% (95% CI, 67–91) at 20 years. Of the additional 6 patients who underwent late MV operation, the initial repair was reimplantation of the anomalous artery in 3 (50% [3 of 6]) patients, Takeuchi repair in 2 (33% [2 of 6]) patients, and ligation of the anomalous artery in 1 (17% [1 of 6]) patient.

Of the 11 patients with severe MR, 5 (45% [5 of 11]) underwent MV repair at the time of ALCAPA repair. In addition 2 (18% [2 of 11]) underwent late MV repair, and 1 (9% [1 of 11]) underwent late MV replacement. The remaining 3 (27% [3 of 11]) patients had mild MR at last follow-up. All patients with preoperative severe MR had normal LV function and either no MR (n = 2) or mild MR (n = 9) at last follow-up.

At most recent follow-up, 16 patients were free of MR and 24 patients had mild MR (Figs 2A, 2B).

Reoperation

Ten patients underwent a total of 11 reoperations at a mean of 9 years (range, 2 months–25 years) after operation. Freedom from any reoperation was 88% ± 7% (95% CI, 74–96) at 5 and 10 years and 76% ± 8% (95% CI, 60–88) at 20 years after operation. Reoperations included MV repair (n = 6), MV replacement (n = 2), and pericardial patch augmentation of the main PA because of stenosis (n = 1) in a patient who underwent a Takeuchi procedure.

![Diagram](https://example.com/diagram.png)

Fig 2. Outcomes of mitral valve (MV) (A) without and (B) with concomitant MV repair at anomalous left coronary artery from the pulmonary artery (ALCAPA) repair.
LV Function

Serial postoperative echocardiograms were available in 32 patients. In these patients, LV function—based on ejection fraction or qualitative assessment—normalized at a median time of 9.5 months (2.3–15.8 months). Echocardiographic reports were available for all 40 patients at last follow-up; LV function was qualitatively assessed as mildly reduced in a total of 4 patients (10% [4 of 40]), whereas all the remaining patients had normal LV function.

Patency of the Coronary Artery

Because all patients were asymptomatic, no routine coronary angiography was performed. All patients who had a Takeuchi repair (n = 12) were asymptomatic at a mean follow-up of 22 years. Two patients underwent coronary angiography at 10 and 23 years after operation, which demonstrated normal coronary arteries. Both of these patients had normal LV function, mild MR, and a negative stress test and were asymptomatic at the time of coronary angiography. Although 2 of these 12 patients required late MV repair (n = 1) or replacement (n = 1), they did not have any evidence of ischemia. After coronary reimplantation (n = 28), all patients were asymptomatic at a mean follow-up of 9 years. All 28 survivors are currently asymptomatic. One asymptomatic patient had coronary angiography at 1 year after operation, which demonstrated normal coronary arteries. Three patients had stress tests at 8, 9, and 15 years after operation, respectively, which were normal. Although 5 patients had late MV repair (n = 4) or replacement (n = 1), they did not have any evidence of ischemia. All 5 patients underwent echocardiography and electrocardiography before repair. All 5 patients had normal LV function and no regional wall motion abnormalities. None had any ischemic changes on electrocardiography. All patients had patency of the proximal LCA confirmed by echocardiography at the most recent follow-up.

Follow-Up

Follow-up was 100% complete for local patients. One international patient was lost to follow-up after returning overseas after the operation. Median follow-up was 14 years (mean, 13 years; range, 4 months–31 years). Thirty-seven patients (93% [37 of 40]) were followed up within the past 5 years. Although 7% (3 of 40) did not have follow-up in the past 5 years, these patients had 7, 10, and 19 years of follow-up, respectively. Twenty-seven patients (68% [27 of 40]) had at least 10 years of follow-up, and 34 patients (85% [34 of 40]) had at least 5 years of follow-up.

Comment

This study demonstrates that surgical repair of ALCAPA can be achieved with good results. Earlier repairs at our institution were through an intrapulmonary baffle described by Takeuchi and associates [4], which was shown to produce no mortality. Despite the low mortality, some patients may experience supravalvular pulmonary stenosis, baffle obstruction, baffle leaks, and aortic regurgitation afterward [14–16]. One patient in this study who underwent a Takeuchi repair required reoperation 7.5 years later because of stenosis of the main PA. After a mean follow-up of 22 years in patients who underwent Takeuchi repairs, we have not encountered any baffle obstructions. All patients since 1995 have undergone reimplantation of the anomalous coronary artery to the aorta at our institution. After a mean follow-up of 9 years in patients who underwent reimplantation, we have not encountered stenosis of the implanted coronary artery.

Early mortality in patients with ALCAPA has been reported to be from 0% to 16% [6, 8–11, 14, 17–21]. Late mortality is rare and survival of 86% to 100% at 10 years has been reported [8, 9, 17, 19]. Mortality from previous studies is summarized in Table 2. An earlier report from our center demonstrated no early or late deaths [6]. We had only 1 early death in our cohort of 43 patients with a median age of 140 days with no late deaths and an overall survival of 98% at 20 years. Edwin and associates [22] reported 27 patients who underwent ALCAPA repair between 1994 and 2011, with a hospital mortality of 3.7% (1 of 27). Seven patients required an LVAD. They determined that a fractional shortening of less than 20% and a cross-clamp time of greater than 56 minutes predicted more than 80% LVAD use. They suggested that in patients with severe LV dysfunction preoperatively, high mortality may result without the use of an LVAD. In our experience, most patients (12 of 15) needed an LVAD because of difficulty weaning from CPB, with a subsequent rise in LA pressure and reduction in mean arterial pressure. In 3 patients, LVADs were used electively. Traditionally, our center has had a low threshold for the use of an LVAD after ALCAPA repair.

Whether to repair the MV at initial repair remains a contentious issue. Several studies reported that concomitant MV repair increases aortic cross-clamp time on an already ischemic myocardium. Although aortic cross-clamp time was significantly higher in patients who
underwent MV repair at ALCAPA repair, this had no effect on the normalization of LV function or other postoperative outcomes. Some surgeons advocate no intervention on the MV at ALCAPA repair, regardless of its severity [6, 14, 23, 24] on the basis that MR often improves postoperatively once coronary blood flow is restored. Kudumula and colleagues [8] described their experience with 25 children who underwent ALCAPA repair between 1990 and 2011 with a policy of addressing only structurally defective MVs. Nineteen patients had preoperative moderate or severe MR, and only 4 patients underwent MV repair at ALCAPA repair because of a structural problem with the MV [8]. They reported no deaths after a median follow-up of 7.8 years, with 4 patients having moderate MR after a median follow-up of 8 years. Conversely, Isomatsu and colleagues [7] described their experience with 29 patients between 1982 and 2000 with a policy of MV repair in all patients with MR. Twenty-four patients underwent MV annuloplasty. They reported 2 early deaths in patients with severe MR, and no late deaths after a mean follow-up of 8.3 years, with an overall survival of 93.1% at 10 years [7]. Additionally, only 1 of the 24 patients who underwent initial MV repair required late MV reoperation. Other centers operate on the MV only if ischemic lesions of the papillary muscles are evident intraoperatively [19], in patients with severe MR particularly in older children [14], or in older children with moderate to severe MR [17].

Despite these various approaches, there are no clearly defined indications for concomitant MV repair at the time of ALCAPA procedures. Of the 11 patients in our study who had severe MR, 5 patients had concomitant MV repair. One of those 5 patients underwent MV reoperation. Of the 6 patients who had severe MR and did not have the concomitant MV repair, 3 required MV repair or replacement during the follow-up period. Therefore 50% (3 of 6) of those patients with untreated severe MR at the time of repair did not require late intervention. Thus overall, 8 of 11 (73%) patients with severe preoperative MR underwent MV repair. Although a definitive recommendation on MV repair cannot be ascertained in this study, if MV repair is deemed to be required at ALCAPA repair, it can be undertaken safely and with good results. Because we did not have adverse outcomes from concomitant MV repair and because 50% of patients with severe MR who did not undergo concomitant MV repair had late MV operation, it seems reasonable to perform concomitant MV repair in those presenting with severe MR. In patients with other degrees of MR, the MR decreases as the ventricular function improves; therefore intervening in these patients does not seem justified. However, because of relatively small numbers, we do not have statistical data to support or refute this opinion.

Limitations
This study is subject to the usual limitations of a retrospective study. Perioperative techniques may have varied during the study period. Statistical analysis of risk factors for mortality was limited because of a relatively small number of patients and outcomes.

The table below shows mortality of ALCAPA repair:

<table>
<thead>
<tr>
<th>Study</th>
<th>Study Period</th>
<th>Patients (n)</th>
<th>Early Deaths (%)</th>
<th>Late Deaths (%)</th>
<th>Concomitant MV Operation (n)</th>
<th>Early Deaths (%)</th>
<th>Late Deaths (%)</th>
<th>Follow-Up (mean, years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schwartz et al [18]</td>
<td>1977–1995</td>
<td>42</td>
<td>14 (6 of 42)</td>
<td>0 (0 of 36)</td>
<td>1</td>
<td>1</td>
<td>0 (0 of 1)</td>
<td>3.7</td>
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<tr>
<td>Huddleston et al [23]</td>
<td>1980–1996</td>
<td>16</td>
<td>6 (4 of 22)</td>
<td>0 (0 of 15)</td>
<td>20</td>
<td>8 (2 of 24)</td>
<td>0 (0 of 1)</td>
<td>6.9</td>
</tr>
<tr>
<td>Isomatsu et al [7]</td>
<td>1982–2000</td>
<td>29</td>
<td>7 (4 of 26)</td>
<td>0 (0 of 27)</td>
<td>4</td>
<td>0 (0 of 23)</td>
<td>0 (0 of 1)</td>
<td>8.3</td>
</tr>
<tr>
<td>Caspi et al [20]</td>
<td>1992–2005</td>
<td>47</td>
<td>9 (4 of 44)</td>
<td>0 (0 of 43)</td>
<td>24</td>
<td>1</td>
<td>0 (0 of 1)</td>
<td>4.7</td>
</tr>
<tr>
<td>Lange et al [11]</td>
<td>1977–2002</td>
<td>56</td>
<td>23</td>
<td>0 (0 of 23)</td>
<td>3</td>
<td>0 (0 of 15)</td>
<td>0 (0 of 1)</td>
<td>6.5</td>
</tr>
<tr>
<td>Brown et al [17]</td>
<td>1975–2007</td>
<td>25</td>
<td>14 (10 of 12)</td>
<td>0 (0 of 13)</td>
<td>0</td>
<td>0 (0 of 3)</td>
<td>0 (0 of 1)</td>
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<td>Ali et al [19]</td>
<td>1986–2007</td>
<td>62</td>
<td>62</td>
<td>0 (0 of 14)</td>
<td>24</td>
<td>10 (6 of 12)</td>
<td>0 (0 of 1)</td>
<td>9.7</td>
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<tr>
<td>Alexi-Meskishvili et al [14]</td>
<td>1992–2010</td>
<td>27</td>
<td>14</td>
<td>0 (0 of 14)</td>
<td>9</td>
<td>0 (0 of 15)</td>
<td>0 (0 of 1)</td>
<td>10.4</td>
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<tr>
<td>Bakhtyari et al [26]</td>
<td>1999–2009</td>
<td>25</td>
<td>18</td>
<td>0 (0 of 15)</td>
<td>0</td>
<td>0 (0 of 23)</td>
<td>0 (0 of 1)</td>
<td>5.0</td>
</tr>
<tr>
<td>Kudumula et al [8]</td>
<td>1990–2011</td>
<td>25</td>
<td>14</td>
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<td>4</td>
<td>0 (0 of 15)</td>
<td>0 (0 of 1)</td>
<td>7.8</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>384</td>
<td>8 (2 of 384)</td>
<td>1 (2 of 384)</td>
<td>47</td>
<td>0 (0 of 47)</td>
<td>0 (0 of 1)</td>
<td>8.0</td>
</tr>
</tbody>
</table>

ALCAPA = anomalous left coronary artery from the pulmonary artery; MV = mitral valve.
Conclusions
ALCAPA can be operated on with good outcomes. Persistent MR and a moderate rate of late MV repair warrants close follow-up.

References

INVITED COMMENTARY
Although not the first to describe this lesion, Edward Bland, Paul White, and Joseph Garland described an infant who died at 3 months of age as a result of this coronary anomaly [1]. For many years this condition was referred to as Bland-Garland-White syndrome before it took on the acronymic term ALCAPA (Anomalous Left Coronary Artery from the Pulmonary Artery). The typical infantile presentation of ALCAPA is characterized by heart failure, a left ventricular ejection fraction of less than 20%, and at least moderate mitral valve regurgitation—certainly not an ideal circumstance to consider any sort of cardiac surgical procedure. Despite this, the results with surgical repair of this lesion are outstanding, and the subsequent recovery of left ventricular function is one of the most remarkable findings in congenital heart surgical practice. Several controversies regarding the specifics of treatment...