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ORIGINAL ARTICLE

Altered Right Ventricular Function in the Long-Term Follow-up Evaluation of Patients After Delayed Aortic Reimplantation of the Anomalous Left Coronary Artery From the Pulmonary Artery

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Abstract This study aimed to evaluate regional and global ventricular functions in the long term after aortic reimplantation of the anomalous left coronary artery from the pulmonary artery (ALCAPA) and to assess whether the time of surgical repair influences ventricular performance.The study examined 20 patients with a median age of 15 years (range 3–37 years) who had a corrected ALCAPA and 20 age-matched control subjects using echocardiography and tissue Doppler imaging (TDI). The median follow-up period after corrective surgery was 6 years (range 2.6–15 years). Seven patients underwent surgery before the age of 3 years (early-surgery group), whereas 13 patients had surgery after that age (late-surgery group). The TDI-derived myocardial strain of the interventricular septum (IVS), lateral wall of the left ventricle (LV), and lateral wall of the right ventricle (RV) in the basal and mid regions were examined, and a mean was calculated. The pulsed Doppler-derived Tei index was used to assess global left ventricular function. No significant differences were found between the early-surgery group and the control group regarding the regional myocardial strain or the Tei index. Compared with the early-surgery group, the late-surgery group had a significantly higher Tei index (mean 0.37; range 0.31–0.42 vs. mean 0.52; range 0.39–0.69; $p < 0.005$), a lower strain percentage of the lateral wall of the LV (mean 29; range 17–30 vs. mean 9; range 7–23), IVS (mean 23; range 21–31 vs. mean 19; range 13–25), and lateral wall of the RV (mean 23; range 21–31 vs. mean 19; range 13–25). The age at operation correlated significantly with the Tei index ($r = 0.84$, $p < 0.001$) and inversely with the mean strain of the lateral wall of the LV ($r = -0.53$, $p = 0.028$), IVS ($r = -0.68$, $p = 0.003$), and lateral wall of the RV ($r = -0.68$, $p = 0.003$). At the midterm follow-up evaluation after corrective surgery of ALCAPA, not only the left but also the right ventricular function seemed to be affected in patients with delayed diagnosis and late surgical repair but preserved among the younger patients with early diagnosis and corrective surgery.

Keywords Aortic reimplantation · Ventricular function · Anomalous left coronary artery from the pulmonary artery · ALCAPA · Tissue Doppler imaging (TDI)

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Introduction

Anomalous origin of the left coronary artery from the pulmonary artery (ALCAPA) is a rare congenital anomaly occurring in 1 of 300.000 births. Also known as the Bland-

White-Garland syndrome, ALCAPA accounts for 0.25–0.5 % of congenital cardiac diseases [8, 10, 12, 13]. The treatment of choice consists of immediate direct reimplantation of the ALCAPA into the aorta and establishment of a dual coronary system [2, 3, 16].

At the long-term follow-up evaluation in previous studies, the focus was on the assessment of global left ventricular (LV) function at rest using conventional echocardiographic techniques that often require geometric assumption [1, 6]. Data on global right ventricular (RV) function is lacking, and data regarding the regional function of both ventricles are sparse [3].

Use of tissue Doppler imaging (TDI)-derived strain, a technique that becomes more or less established in daily clinical practice, is useful in this clinical setting because it provides information on regional and global myocardial deformation without the need for geometric assumption [9, 19].This study aimed to evaluate global and regional myocardial functions at the midterm after aortic reimplantation of an ALCAPA using TDI-derived strain and to assess the effect that timing of surgical repair has on the long-term ventricular performance in this group of patients.

Materials and Methods

Subject Population

This study investigated 20 consecutive adults and children with ALCAPA who underwent successful surgical treatment at the Deutsches Herzzentrum Berlin by direct reimplantation of the anomalous left coronary artery into the aorta and came to outpatient visits at least once a year. Data obtained from these patients were compared with the data for 20 age-matched healthy children undergoing cardiac examination to exclude congenital cardiac malformation (group 1).

The median age of the patients at corrective surgery was 48 months (range 4–372 months). Whereas seven patients had surgery before the age of 3 years (early-surgery group, group 2), 13 patients had surgery after the age of 3 years (late-surgery group, group 3). The median follow-up period was 5.2 years (range 4.8–10.5 years) for the early-surgery group and 9.5 years (range 4–15 years) for the late-surgery group. The operative technique and the early results for these patients have been reported previously [1–3].

All the patients in group 1 underwent an emergency operation due to symptoms of severe LV dysfunction and congestive heart failure. Six of these infants were intubated and mechanically ventilated for 1–6 days before the operation because of cardiopulmonary instability, with resuscitation in two of these cases. All the older children (age >3 years) underwent elective surgery.

Nine patients (3 from group 2 and 6 from group 3) with grade 3 or 4 mitral valve regurgitation underwent a modified Kay-Wooler (five patients) or Paneth (four patients) mitral annuloplasty combined with giant left atrium plication in one case and with shortening of elongated chordae in two cases.

Standard Echocardiography

Both the control subjects and the ALCAPA patients were examined by echocardiography using a 2.5- to 3.5-MHz transducer (GE Vingmed System VII Ultrasound Scanner, General Electrics, Fairfield, Connecticut, US; Horten, Norway). Cross-sectional echocardiography with appropriate M-mode measurements of the LV ejection fraction was performed. Color, pulsed, and continuous Doppler was used to detect residual valve dysfunction.

Determination of LV Global Function Using the Pulsed Doppler-Derived Tei Index

Pulsed Doppler flow across the mitral and aortic valves was assessed with simultaneous electrocardiographic (ECG) recordings for each patient. The usual size of the pulsed Doppler gate was 1.5 mm, and the filter was adjusted to 100 Hz. For optimal acquisition, care was taken to direct the transducer beam as closely as possible to the Doppler beam, at less than 20° in selected planes. No angle correction was performed. In the apical four-chamber view, the mitral valve inflow velocity profiles were recorded with the Doppler sample placed at the tip of the mitral valve. The Tei index was calculated as previously described [17].

Tissue Doppler Imaging for Analyzing Regional Ventricular Function

Afterward, the subject collective underwent a color Doppler myocardial imaging (CDMI) study, during which the longitudinal function was recorded from the RV free wall, the interventricular septum (IVS), and the LV lateral wall using the standard apical four-chamber view [19]. All data were acquired at a high frame rate of 180 ± 15 frames/s. An appropriate velocity scale was chosen to avoid data aliasing. Care was taken to keep each wall in the center of the ultrasound sector in an attempt to align it as near zero degrees as possible to longitudinal motion.

Three consecutive cardiac cycles (to be used for subsequent analysis) were recorded during normal quiet respiration. The CDMI data were stored in digital format and transferred to a computer workstation for the offline analysis of regional myocardial strain (deformation) curves. Strain was estimated by measuring the spatial velocity gradient over a computation area 9 mm in a longitudinal direction.

The TDI-derived myocardial strain of the IVS, the left lateral ventricular wall, and the right lateral ventricular wall in the basal and mid regions were examined, and a mean was calculated. This was performed using dedicated software (Echopack 6.2.3; GE Vingmed).

Statistical Methods

All values are expressed as medians and ranges. The Mann–Whitney U test was used to assess the difference between the means of two unpaired groups. For the analysis of correlation, the nonparametric Spearman rank correlation was performed. A p value lower than 0.05 was considered statistically significant.

Results

Physical Examination and Standard Echocardiographic Measurements

All the patients were free of symptoms, and 17 were classified as New York Heart Association (NYHA) I, whereas three patients were classified as NYHA II (all in group 3). Antegrade flow in the reimplanted coronary artery was documented by echocardiography in all the patients. Four patients (2 from group 2 and 2 from group 3) had mitral regurgitation grade II, whereas the remainder of the examined patients had either no or mild mitral regurgitation. None of the examined patients had significant aortic regurgitation or pulmonary stenosis. The median ejection fraction of the LV among the ALCAPA group was 68 (range 63–84 %).

Within the patient cohort, no significant difference was found between the early- and late-surgery groups regarding the calculated ejection fraction. In contrast, the Tei index was abnormally elevated ($p = 0.004$) in late-surgery group (0.36 ± 0.044) compared with the early-surgery group (0.53 ± 0.08) ($p = 0.004$) (Fig. 1). Moreover, the Tei index correlated significantly with age at the operation ($r = 0.83$, $p < 0.001$).

Tissue Doppler Imaging for Analyzing Regional Ventricular Function

Comparing the early-surgery group with the control group, the regional myocardial strain did not differ significantly in any of the examined segments of the RV, LV, or IVS (Table 1). On the other hand, the late-surgery group had a significantly reduced regional strain compared with the early-surgery group in all the examined segments (Table 1; Figs. 2, 3). A negative correlation was found between the age of the patients at surgery and the mean strain of LV ($r = -0.53$, $p = 0.028$), IVS ($r = -0.68$, $p = 0.003$), and RV ($r = -0.68$, $p = 0.003$).

Discussion

The data in the literature regarding mid- and long-term postoperative LV function in patients with ALCPA differ substantially. Studies using conventional echocardiography have reported normal LV function after surgical correction [14]. However, a diminished coronary artery flow reserve was reported in a study using positron emission tomography [15].

In the current study, using conventional echo parameters such as the ejection fraction, no statistically significance difference was found between the patients and the control subjects. However, when TDI-derived strain and the Tei index (parameters that need no geometric assumption) are used to evaluate regional and global LV function, our data showed that in the mid- to long-term follow-up evaluation after surgical correction of ALCAPA, both the regional and global LV function is reduced in patients with late diagnosis and surgical correction, whereas it is preserved in patients who have surgery at a relatively early age (Figs. 1, 2, 3). This may indicate that for ALCAPA patients, the age at surgical repair has an important influence on residual myocardial injury and thus on long-term postoperative ventricular performance.

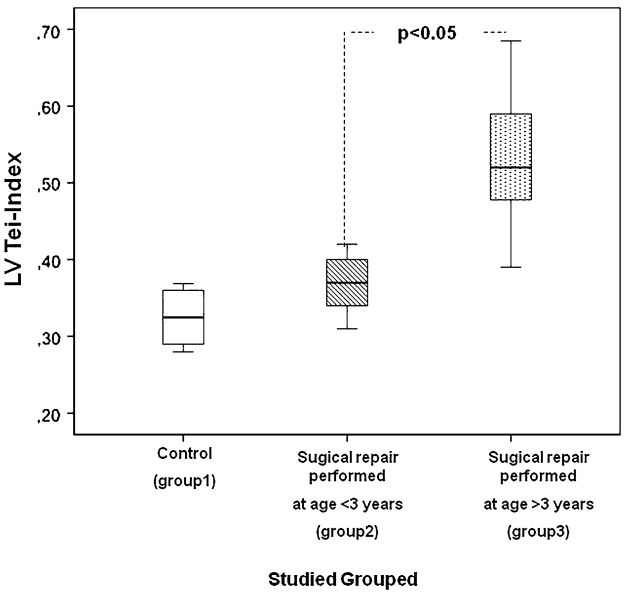

Fig. 1 Comparison of control subjects and patients after ALCAPA repair in terms of LV global function assessed by the Tei index. The early-surgery patients are those who had surgical repair before the age of 3 years, and the late-surgery patients are those who had surgical repair after the age of 3 years. ALCAPA, anomalous origin of the left coronary artery from the pulmonary artery

Table 1 Comparison between control subjects and patients after ALCAPA repair regarding regional and global ventricular functions

Parameter	Control group (group 1) ($n = 20$) *n* (range)	Early-surgery ALCAPA patients (group 2) ($n = 7$) *n* (range)	Late-surgery ALCAPA patients (group 3) ($n = 13$) *n* (range)
LVEF (%)	73 (68–75)	72 (63–84)	68 (63–77)
LV Tei index	0.33 (0.28–0.37)	0.37 (0.31–0.42)	0.52 (0.39–0.69)[a,b]
Basal LV strain (%)	25(15–35)	27 (18–33)	11 (4–24)[a,b]
Mid LV strain (%)	28 (18–36)	25 (16–32)	9 (5–23)[a,b]
Mean LV strain (%)	26 (17–36)	29 (17–30)	9 (7–23)[a,b]
Basal IVS strain (%)	24 (21–30)	22 (20–33)	18 (14–27)[a,b]
Mid IVS strain (%)	27 (24–30)	26 (21–29)	18 (11–23)[a,b]
Mean IVS strain (%)	26 (24–27)	23 (21–31)	19 (13–25)[a,b]
Basal RV strain (%)	30 (25–37)	30 (22–34)	23 (12–30)[a,b]
Mid RV strain (%)	31 (28–37)	30 (25–37)	23 (14–33)[a,b]
Mean RV Strain (%)	26 (24–27)	23 (21–31)	19 (13–25)[a,b]

ALCAPA anomalous origin of the left coronary artery from the pulmonary artery, *LVEF* left ventricular ejection fraction, *LV* left ventricle, *IVS* interventricular septum, *RV* right ventricle

[a] Late-surgery (age >3 years) versus early-surgery (age <3 years) patients with ALCAPA ($p < 0.05$)

[b] Late-surgery versus normal patients with ALCAPA ($p < 0.05$)

The preserved postoperative ventricular performance among early-surgery patients can be explained by the phenomenon of hibernation, which refers to the presence of chronic LV hypoperfusion that could be improved after revascularization [5]. The reduced regional and global ventricular functions among the late-surgery patients could be explained by irreversible regional myocardial damage, which may be associated with persistent perfusion defects frequently seen in patients who have surgical repair late rather than early [16].

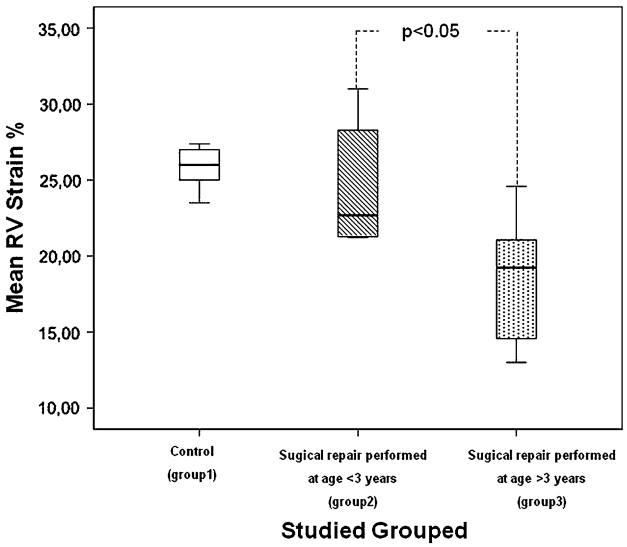

Fig. 2 Comparison of control subjects and patients after ALCAPA repair in terms of right ventricular (RV) deformation. The early-surgery patients are those who had surgical repair before the age of 3 years, and the late-surgery patients are those who had surgical repair after the age of 3 years. ALCAPA, anomalous origin of the left coronary artery from the pulmonary artery

To our knowledge, this is the first report demonstrating that the longitudinal RV function among ALCAPA patients with late surgery is reduced, whereas it is preserved among patients with early surgery. Patients who underwent late surgery had well-developed collaterals between the right and left coronary arteries as well as large extracardiac collaterals. Before surgery, these collaterals may lead to significant steal phenomena from the right to the left coronary system at the cost of right myocardial perfusion.

In addition, these collaterals may lead to extensive washout of the cardioplegic solution during the corrective surgery, which may result in incomplete RV myocardial protection [2]. Clinicians also should not ignore the fact that the RV free wall is composed largely of subendocardial longitudinal muscle fibers [5], which are particularly susceptible to the deleterious effect of cardiopulmonary bypass and intraoperative procedure [4, 11].

Secondary to this steal phenomenon, chronic hypoperfusion of the right myocardium in the late-surgery patients also may occur [15]. Di Salvo et al. [7] reported preserved RV function after ALCAPA repair using tissue Doppler-derived strain. However, most of the patients included in their study underwent surgery before the age of 1 year. This may further demonstrate the role of early surgery in preservation of the RV function in patients with ALCAPA.

Study Limitations

A limitation of this study was its cross-sectional and non-longitudinal character. Absence of preoperative data from

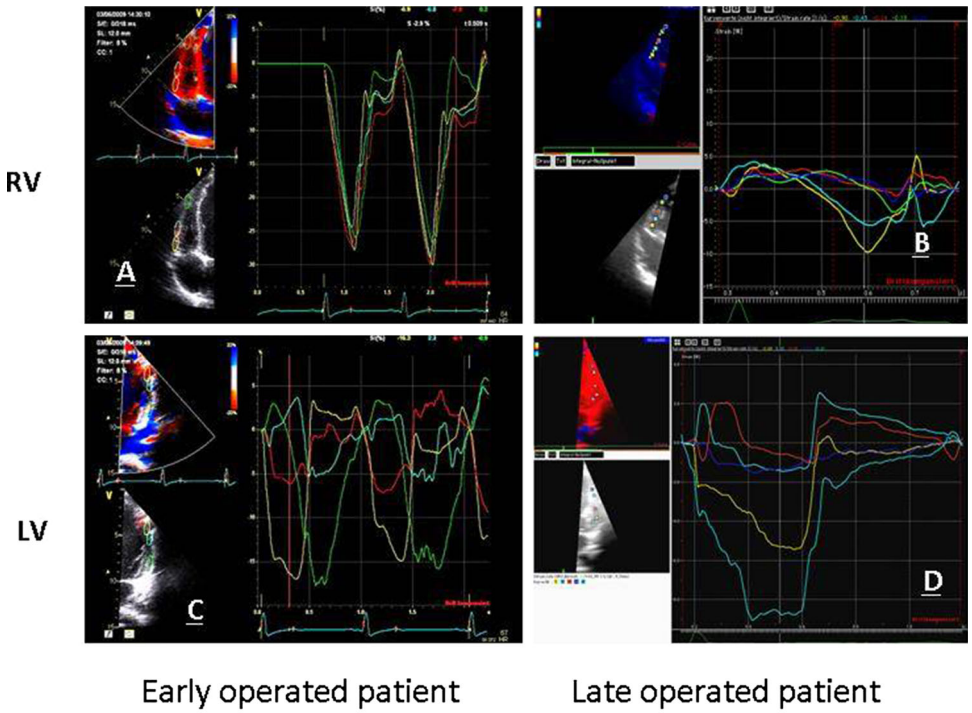

Fig. 3 Right and left ventricular regional strain values in the early-surgery patients (**a**, **c**) and late-surgery patients (**b**, **d**). The lower regional strain values in both the LV and RV were found in the long-term follow-up evaluation of the late-surgery rather than the early-surgery patients

tissue Doppler and the Tei index make it impossible to compare the preoperative ventricular function between the early- and late-surgery groups.

Two-dimensional (2D) strain obtained through speckle tracking is a novel method considered superior to one-dimensional Doppler-derived strain in some aspects [18]. However, adequate 2D image quality is crucial to reliable speckle tracking, which could be challenging for postoperative ALCAPA patients, especially when they reach adult ages. Instead, TDI may have some immunity to poor image quality [20]. Unlike TDI velocity, TDI-derived strain is less affected by cardiac translation or a tethering effect but keeps the same high frame rate.

Conclusion

Long-term follow-up evaluation of clinically asymptomatic patients after surgical correction of ALCAPA shows that not only the left but also the regional and global RV functions assessed by TDI is reduced in those patients with late correction but preserved among patients who have surgery at an early age. Early diagnosis and surgical treatment by means of revascularization in neonates and infants with ALCAPA is warranted and may influence the long-term outcome of global and regional myocardial performance in the left and right ventricles. In addition, such latent myocardial dysfunction was detectable using the TDI rather than the conventional echocardiography methods.

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Conflict of interest The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

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