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Comparative Analysis of Left Ventricular Myocardial Strain in Children with Cardiac Allograft Vasculopathy after Heart Transplantation

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Abstracts

Background: Cardiac allograft vasculopathy (CAV) is a major complication of cardiac transplantation and causes up to 25% of the late deaths in children who undergo this procedure. Recently, strain imaging studies using speckle tracking echocardiography have been performed to screen for CAV in heart transplant recipients but this has primarily been in adult patients. We here investigated the possibility of using LV myocardial strain as an alternative screening method for CAV in pediatric heart transplant patients.

Methods: This study included 71 children who underwent a heart transplantation at Asan Medical Center between August 1997 and June 2017. These subjects were stratified by the presence or absence of CAV on intravenous ultrasound (IVUS). CAV was defined as a coronary artery intimal thickness above 0.5 mm. The echocardiography and catheterization data which was measured at 1 year post-transplantation were compared between two groups.

Results: The LV global longitudinal strain (LVGLS) values were significantly higher in the patients without CAV (-15.8%±3.85% in the CAV(-) group vs -11.52%±3.78% in the CAV(+) group; p-value <0.01). ROC curve analysis an LVGLS threshold of -14.03% was also found to be predictive of CAV with a sensitivity and specificity

of 73.3% and 80%, respectively.

Conclusion: In this study, children who develop CAV following heart transplantation showed deteriorated myocardial deformation. Strain analysis might be considered as an alternative CAV evaluation tool for pediatric heart recipients in whom angiography is limited.

Key words : Heart transplant, Pediatric, Cardiac allograft vasculopathy, Myocardial Strain analysis

Introduction

Successful long-term outcomes have been achieved for pediatric heart transplant recipients, including a 10 year survival rate of approximately 60% according to the International Society for Heart and Lung Transplantation (ISHLT) registry.[1)]

It is note that cardiac allograft vasculopathy (CAV) is a leading cause of long-term mortality in heart transplant recipients, accounting for up to 1 in 8 deaths beyond one year post-transplant.[2)] In children undergoing cardiac transplantation however, CAV is actually the cause of 1 in 4 late deaths.[3)] based on ISHLT registry data, 60% of pediatric cardiac recipients are free of CAV at 11 years post –heart transplant. Once CAV is detected however, graft survival is only 48% at 5 years post-diagnosis.[1)]

The importance of early CAV detection has been emphasized as this is an adverse prognostic indicator.[4)] However, it remains difficult to detect CAV with selective coronary angiography, the current gold standard for diagnosing CAV with high specificity, but of moderate sensitivity, due largely to its manner of presentation and the technical difficulties of diagnosing CAV in children.[5, 6)] CAV involves the epicardial vessels and the coronary microvascular system and presents as characteristic diffuse concentric intimal thickening.[7)] Although, the intravascular ultrasound (IVUS) modality is a more sensitive approach and is thus

more effective in the early detection of CAV and progression monitoring [8], its use in children has lacked universal acceptance, partly because of its invasive nature, perceived risk, and the significant costs involved.[3] An alternative non-invasive modality to evaluate the presence of CAV in children, which could decrease the frequency of cardiac catheterization, is thus needed.

A conventional echocardiographic assessment of left ventricular function is a well established method for routine graft function monitoring.[9, 10] This evaluation tool has some limitations however in terms of screening for deteriorating graft function due to CAV.[7, 11] In this regard, the well-established left ventricular global longitudinal strain (LVGLS) is a relatively easy, robust and simple method of measuring a longitudinal myocardial deformation. Moreover, a significant correlation between LVGLS and CAV in cardiac transplant patients has been reported in previous studies.[7, 12] However, whether the onset of CAV induces any significant change in myocardial strain is still unclear.[13] Although LV mechanics evaluated with speckle tracking imaging (STI) might provide insight into the extent of CAV,[14] few studies to date have assessed the relationship between CAV and strain analysis in young heart transplant recipients.

We aimed in our present analysis to investigate the possibility of utilizing echocardiographic LV myocardial speckle strain analysis as an alternative

screening method for CAV in pediatric heart transplant patients.

Methods

Subjects

A total series of 91 pediatric patients who were under 18 years old and underwent a heart transplantation at Asan Medical Center between August 1997 and June 2017 were retrospectively reviewed for inclusion in this study. The medical records of this patients series were reviewed for the presence of CAV and for echocardiographic parameters including strain imaging analysis at 1 year-post transplantation. Any patient who expired within 1 year of their procedure or who had not been evaluated for CAV or received an echocardiographic cardiac function test at 1 year post-transplantation was excluded. Patients were divided into two groups by the presence of CAV, defined by a coronary artery intimal thickness of above 0.5 mm. The patients whose coronary artery intimal thickness of above 0.5 mm were classified as group of patients with significant CAV (CAV(+) group) and the other patients were classified as group of patients without significant CAV (CAV(-) group). All patients had been managed with a calcineurin inhibitor based maintenance immunosuppression regimen.

Echocardiography

Echocardiographic studies were performed according to the post heart transplantation screening protocol of Asan Medical Center using commercially available ultrasound equipment including a Philips IE33 system (Phillips Medical Systems, Andover, MA) and General Electric Vivid E9 device (GE Health Medical, Horten, Norway). Probe frequency was at the discretion of the sonographer depending on the size and age of the patient. Each study included a short-axis image through the left ventricle at the level of the mitral valve, papillary muscles and apex. In addition, an apical two, three and four-chamber image were included in every evaluation. These images were used for speckle-tracking imaging. Among the echocardiographic data which had been serially conducted in every patient, those that were closet in terms of timing to the angiographic analysis were selected. In most patients, the echocardiographic study was conducted in the following day of angiographic study. All echocardiographic data were reviewed retrospectively.

Speckle-Tracking Echocardiography

Two-dimensional speckle-tracking analysis was conducted using TomTec (TomTec

Imaging Systems; GmbH, Unterschleissheim, Germany) on echocardiograms that were generated on the day after the endomyocardial biopsy.

Longitudinal strain analysis was performed using an apical two, three and four-chamber image and the mean values obtained from this analysis were then defined as the LVGLS values. The GLS was calculated using software as the average longitudinal systolic strain of 17 myocardial segments at the time in systole when the value peaked. Circumferential strain analysis was performed using a parasternal short-axis image at the level of the mitral valve, papillary muscles and apex. The mean values from this analysis were then defined as the LVGCS values. The RV global longitudinal strain (RVGLS) was analyzed in the four-chamber view and calculated using software as the average of three regional peak systolic strains measurements along the entire RV free wall (basal, middle, and apical). The speckle area of interest was manually adjusted for optimal tracking results and any inadequate images of ventricular segment tracking were excluded from this analysis.

Data were stored digitally and analyzed offline by an investigator (K.M.J) who was blind to the clinical status, CAV status, and biopsy results for the patient. Analysis was performed by a single reader. The intraclass correlation coefficient (ICC) for the intraobserver GLS and GCS was calculated with the primary

investigator performing measurements; All GLS and GCS images were reviewed again.

Catheterization Parameters

All of the study patients underwent catheterization at one-year after transplantation in accordance with the routine post heart transplantation management protocol of our hospital. The data extracted from these catheterizations included the presence of CAV, mean pulmonary artery pressure, left ventricular end-diastolic pressure and right ventricular end-diastolic pressure. The presence of significant CAV in this study was defined by an intimal media thickness of above 0.5 mm, as determined by IVUS.[15)]

Acute Allograft Rejection

A clinical rejection of transplanted heart requiring intervention is defined by evidence of a compromised LV systolic function on conventional echocardiography or by histopathological evidence of an acute allograft rejection of above grade 2 on myocardial biopsy at one month post-transplantation. In such instances, the affected patients underwent immune modulation therapy which was mainly steroid pulse therapy. All echocardiographic data in our heart

transplant recipients were acquired either during a rejection-free status period, at least one month after treatment for acute rejection or in cases with no documented evidence of acute rejection during the month prior to the echocardiographic evaluation.

Statistical Analysis

Continuous data are presented as a mean ± standard deviation and categorical data as a frequency or percentage. Catheterization, 2-dimensional echocardiographic parameters, and previously described strain parameters were compared between subjects with and without CAV using Student's t tests. Statistical analyses were performed using SPSS version 21. A p value<0.05 was considered indicative of statistical significance. The intraclass correlation coefficient (ICC) was calculated to assess intraobserver variability. Intraobserver agreement was relatively higher for LVGLS(0.894) and LVGCS(0.884).

Results

Subjects Characteristics

Of the 91 pediatric cardiac transplant recipients that were screened initially, 71 patients were included in the study cohort for further analysis. Of the 20 patients

who were excluded, 9 had died within one year of transplantation, one patient had not been followed-up at the out-patient clinic, 6 children had only poor quality echocardiographic data, and 4 patients had not yet undergone a one year post-transplant evaluation yet. Twenty eight patients were classified as CAV(+) group and the other 43 patients were classified as CAV(-) group. The Baseline demographics of the subject population are summarized in Table 1.

The mean intimal thickness on IVUS was significantly higher in CAV(+) group than in CAV(-) group (0.97 ± 0.41mm vs 0.3 ± 0.8, $p<0.01$). No significant difference was observed in the sex ratio between the groups. Although the mean age at transplantation was higher in CAV(-) group (11.3 ± 5.5 years old vs 11.1 ±5.5 years old, $p=0.01$), the body weight at transplantation was higher in CAV(+) group (31.79 ± 18.99 vs 41.87 ± 19.09, $p=0.04$). The rejection rate was comparable in both groups (18.6% vs 17.8%) but the post heart transplantation mortality rate was higher in CAV(+) group.

Comparison of Baseline Echocardiographic and Catheterization Parameters According to the Presence of CAV

The baseline echocardiographic and catheterization data were collected for the

Table 1. Baseline Demographic Characteristics of Subjects

Demographic data	**CAV(-) (N=43) Mean ± SD**	**CAV(+) (N=28) Mean ± SD**	**P value**
Male gender	53.5 %	67.9 %	
Age at transplant (years)	11.3 ±5.5	11.1 ± 5.5	0.01
Body weight at transplant (Kg)	31.79±18.99	41.87 ±19.09	0.04
Rejection episode	18.6 %	17.8 %	
Episodes/person	0.35	0.29	
Post transplantation mortality rate	9.3 %	21.4 %	
CAV	0.30 ± 0.08	0.97 ± 0.41	<0.01

heart transplant children in both groups, and had been measured at one month post-transplantation in accordance with the management protocol of our hospital. There were no significant differences found between the 2D echocardiographic or strain parameters in the two groups at baseline other than the LV mass index (119.38±40.9 in CAV(-) vs 127.16±44.47 in CAV(+); p=0.04). In addition, no statistical difference was evident for the catheterization parameter between two groups. These results are listed in Table 2.

Table 2. Baseline Echocardiographic and Catheterization Parameters of the Patients One-Month Following Heart Transplantation

Baseline demographic data	**CAV(-) (N=43) Mean ± SD**	**CAV(+) (N=28) Mean ± SD**	**P value**
Baseline echocardiographic data			
LVEDD (mm)	38.42±7.94	38.66±5.29	0.89
LV fractional shortening (%)	37.98±6.70	38.98±6.38	0.53
LV mass index (g/m^2)	119.38±40.99	127.16±44.47	0.04
E/A ratio	1.75±0.57	1.70±0.30	0.72
LVEDV (mL)	62.48±28.58	68.55±24.81	0.37
LVEF (%)	67.88±8.7	68.23±7.56	0.86
LVGLS* (%/sec)	-11.58±4.17	-8.73±4.93	0.05
LVGCS† (%/sec)	-23.72±7.16	-24.03±3.86	0.87
RVGLS‡ (%/sec)	-6.5±6.6	-7.13±6.33	0.77
Baseline catheterization data			
Mean pulmonary artery pressure(mmHg)	21.0±5.29	15.86±4.26	0.08
LVEDP	10.0±5.59	8.57±2.93	0.57
RVEDP	7.31±4.13	6.13±5.00	0.56

Baseline measurement values are the result of 1 month after transplantation

*LV global longitudinal strain, †LV global circumferential strain, ‡RV global longitudinal strain

Comparison of One Year-Post Transplant Echocardiographic and Catheterization Parameters According to the Presence of CAV

Echocardiographic and angiographic analysis were conducted in all study subjects one year after transplantation as a routine part of the post heart transplantation management protocol of Asan Medical Center. At baseline, the children who subsequently developed CAV in CAV(+) group had similar traditional echocardiographic function and strain parameters in comparison with the cases in CAV(-) group. However, significant lowering of the LVGLS was observed in the CAV(+) group cases at one year post-transplantation (-15.8±3.85 in the CAV(-) group vs -11.52±3.78% in the CAV(+) group, $p<0.01$) indicating a deterioration of LVGLS in this parameter in patients with potential of CAV developing. However, significant differences were seen only in the catheterization parameter. These results are presented in Table 3.

Correlation of CAV and Echocardiographic Parameters

Pearson correlation analysis was performed to identify any relationship between coronary artery intimal thickness and echocardiographic parameters, including strain parameters. In evaluating valid parameter for predicting CAV, no definite positive correlation was observed between LVGLS and CAV (correlation

Table 3. Post Transplantation Echocardiographic and Catheterization Parameters of the Patients One-Year after Heart Transplantation

Post transplantation demographic data	**CAV(-) (N=43) Mean ± SD**	**CAV(+) (N=28) Mean ± SD**	**P value**
Echocardiographic data			
LVEDD (mm)	37.9±7.44	39.45±5.6	0.36
LV fractional shortening (%)	37.79±6.98	39.9±7.98	0.29
LV mass index (g/m^2)	95.12±31.83	97.82±31.69	0.73
E/A ratio	1.75±0.57	1.73±0.44	0.88
LVEDV (mL)	62.7±25.8	71.41±19.18	0.14
LVEF (%)	67.34±11.4	68.48±10.44	0.68
LVGLS* (%)	-15.8±3.85	-11.52±3.78	<0.01
LVGCS† (%)	-20.62±5.1	-24.04±6.79	0.08
RVGLS‡ (%)	-9.51±5.92	-6.59±6.2	0.17
Catheterization data			
Mean pulmonary artery pressure (mmHg)	18.0±9.47	16.8±6.34	0.76
LVEDP	11.63±6.89	9.36±3.89	0.32
RVEDP	6.09±5.22	6.36±4.01	0.89

Post transplantation measurement values are the result of 1 year after transplantation.

*LV global longitudinal strain, †LV global circumferential strain, ‡RV global longitudinal strain

coefficient=0.648, p=0.08). (Figure 1) Receiver operating characteristic curves were generated to determine a threshold value for changes in the echocardiographic measurements including strain parameters associated with CAV development. An LVGLS threshold of -14.03 led to a sensitivity of 73.3% and a specificity of 80% for the development of CAV (area under the curve 0.800, 95% CI, 0.65 to 0.95; p <0.01). (Figure 2)

Discussion

We attempted in our current analysis to evaluate the change of myocardial strain in pediatric HT patients with significant CAV and verify whether myocardial strain analysis was a viable alternative to an invasive angiography for detecting CAV. As a result, we identified a decreased LVGLS, which indicates LV myocardial deformation and deterioration of function in these significant CAV cases.

Current gold standard method of diagnosing CAV is selective coronary angiography.[16] However, for some reasons, angiographic diagnosis criteria for CAV in pediatric patients was not always confirmative.[5] The current ISHLT consensus regarding CAV may not always be appropriate in children.[5] There are potential differences in CAV types between children and adult heart transplant recipients such as less common discrete proximal coronary artery lesions and

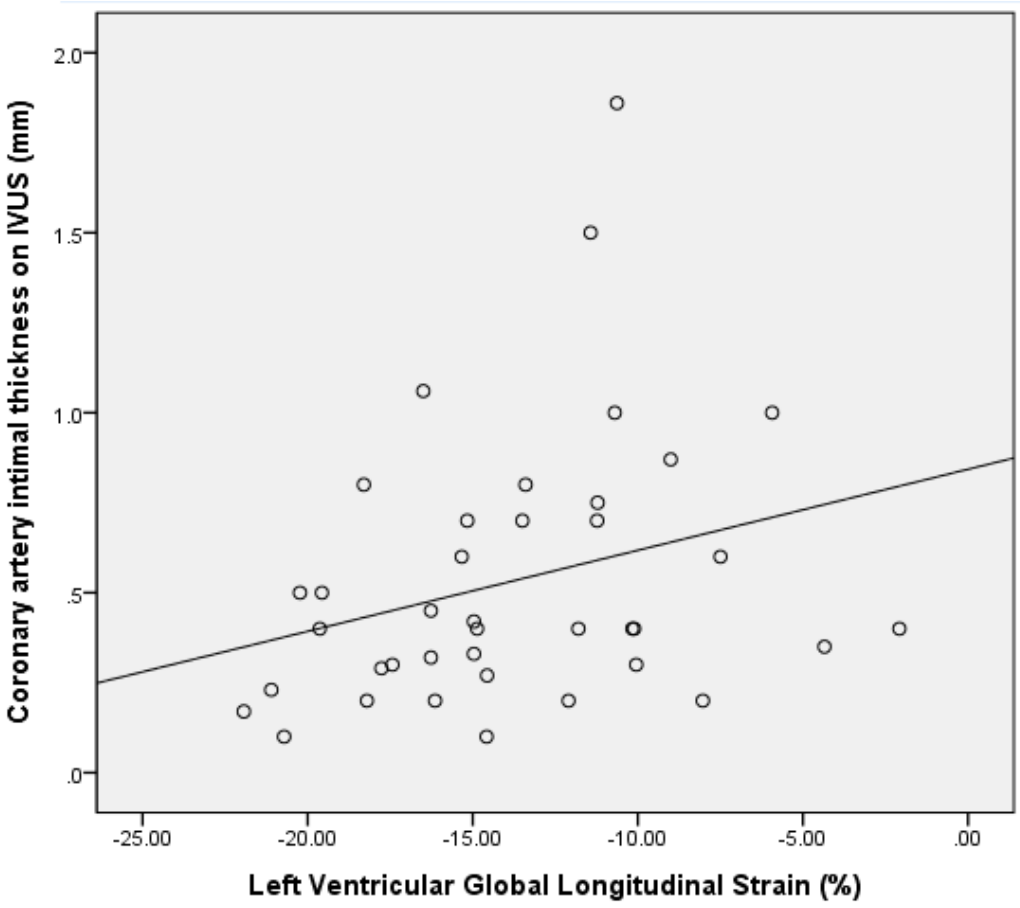

Fig. 1. Pearson correlation analysis between CAV and LVGLS.

Tendency of positive correlation was observed between LVGLS and coronary artery intimal thickness on IVUS (mm) measured at 1 year after heart transplantation (correlation coefficient=0.648, P=0.08).

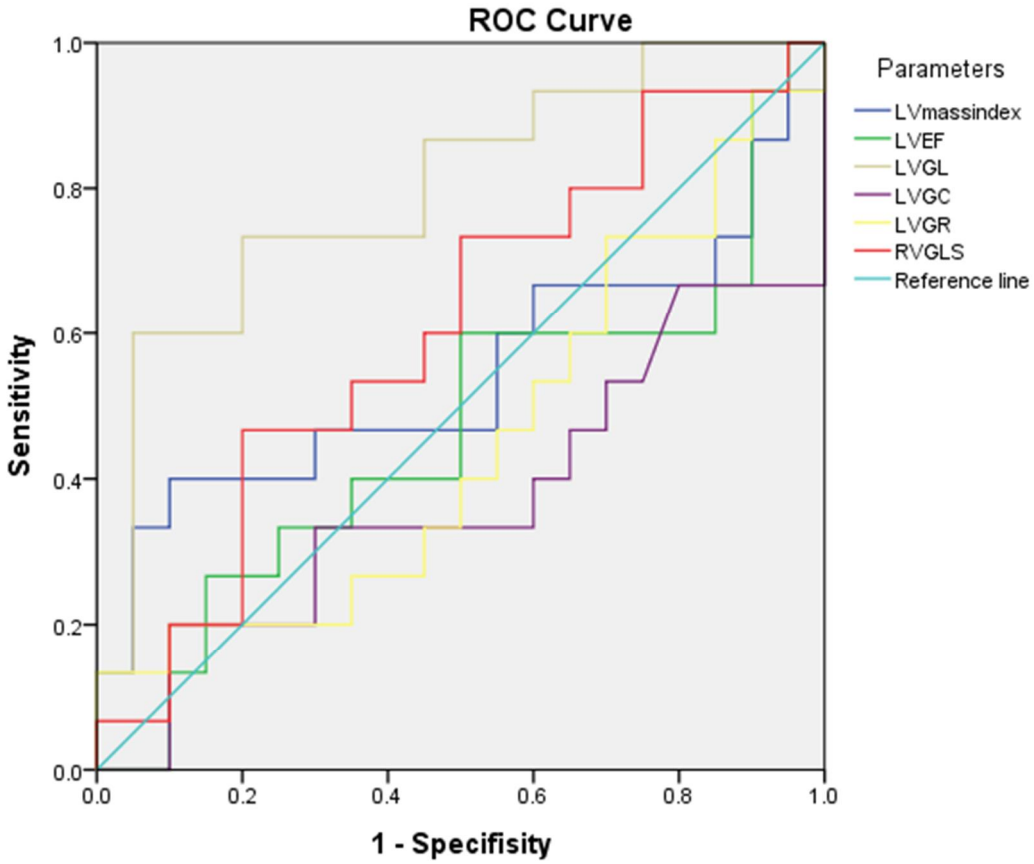

Fig. 2. Receiver operating curves of the Echocardiographic Parameters and CAV.

Area under the curve of LVGLS is 0.800 (95% CI, 0.65 to 0.95; p <0.01), most high value compared to others echocardiographic parameters with sensitivity of 73.3% and specificity of 80.0%.

predominant diffuse distal disease.[5] There are also variable anatomic classification/scoring systems have limited consistency.[16] This is why previous studies have adopted the concept of significant CAV in accordance with the maximal coronary artery intimal thickness on an IVUS image, and not the classical ISHLT criteria for this condition, to classify the patients for prognostic evaluation.[17, 18] M. Fenton et al also adopted this concept to define significant CAV in 2 previous studies for pediatric heart transplantation patients.[3, 15] For this reason, the patients with significant CAV have been defined according to a maximal intimal thickness >0.5 mm in our present study.[19]

However, for its coronary angiography-based characteristics, IVUS as well as selective angiography necessarily has some limitation, especially in small children. Selective coronary angiography procedure may be technically difficult and high risk in very small children with a body weight of below 10 kg.[5] Technical challenges with coronary angiogram in infants, younger patients, and cases with a history of complex congenital heart disease, the value of the diagnostic yield and potential clinical impacts from a procedural risk-benefit perspective should be considered.

The technical limitations to IVUS in the pediatric population also remain a challenge with the lower weight limit in the literature ranges from 10 to 25 kg;

there is still sporadic use in children for its inherent potential risks which can include coronary artery spasm, dissection and/or catheter complications.[8, 16, 20-22] Moreover, considering the biphasic pattern of CAV progression, angiographic diagnosis may not detect subtle changes in epicardial vasculopathy or small vessel disease well. Despite its limitations, a great part of centers still rely on coronary artery angiography as the "gold standard" for diagnosis of CAV.

In efforts to develop alternate methods of CAV screening, several previous studies have reported that myocardial strain deterioration occurs in patients with CAV.[7, 13] T. S. Clemmensen et al. reported significantly reduced LVGLS in heart transplantation patients according to the degree of CAV.[7] However, the results of those reports were inconsistent, and could not be confirmed.[13] The deterioration of LVGLS in post HT patients with CAV have not been shown significance in other study.[13]

With the regard to the pathophysiology of CAV progression, and even though the precise etiology of CAV remains elusive, previous studies have suggested underlying immunologic mechanisms triggered by immune-independent factors such as ischemia–reperfusion injury, infections, and metabolic disorders.[23] The donor endothelium is the principal target of this immune cascade which results in the proliferation and differentiation of inflammatory/immune cells via

inflammatory cytokine release.[24] These alloimmune responses consequently leads to endothelial damage, causing complement activation and fibrin deposition.[24] Moreover, they may lead not only to donor cell death but also more chronic processes that trigger smooth muscle cell proliferation, intima-medial thickening, and ultimately a reduction in the luminal area throughout the donor vasculature.[25] Such luminal narrowing, a characteristic feature of CAV, may induce ischemic damage of myocardium via a reduced coronary artery blood flow, resulting in detrimental changes to echocardiographic parameters, especially myocardial strain.

Previous studies have demonstrated the high prognostic value of strain in the early phases after a heart transplantation.[26, 27] The magnitude of an LVGLS measurement is highly dependent on the contraction of longitudinally oriented myocardial fibers. Most of these fibers are located in the endocardium. Consequently, the LVGLS value is significantly affected by perfusion abnormalities, left ventricular wall stress abnormalities, myocardial fibrosis, and myocardial edema. CAV is known to affect both epicardial vessels and microvascular function. The effects of CAV on both of these vascular compartments leads to perfusion abnormalities and subsequently to a potentially reduced LVGLS.[12] In heart transplant recipients, the surgical procedure, ischemic transport damage, LV

remodeling, rejection, hypertension, fibrosis due to immunosuppressive treatment, and impaired microvascular and macrovascular perfusion are all possible contributors to the induction of impaired longitudinal systolic function.[28, 29]

Decreased myocardial deformation analyzed with speckle tracking echocardiography analysis was reported in several previous studies of pediatric cardiac transplantation patients.[30, 31] However, those prior studies were focused on a comparison of myocardial strain analysis with conventional echocardiography in patients showing graft rejection[31] or although a diminished myocardial strain associated with CAV in other reposts, no cutoff value was suggested for a left ventricular strain that would enable this analysis to be a potential alternative screening tool for CAV.[30, 32] However, despite a number of confounders, we have demonstrated that LVGLS is the best echocardiographic parameter for detecting myocardial dysfunction related to CAV and also suggest a threshold of -14.03% to assess CAV in pediatric cardiac transplantation patients. Since normal reference range of LVGLS in post heart transplantation was suggested only in adult recipients (LVGLS between –16.5% and 18% is considered to be normal in stable heart transplant patients.[7]) this is the 1st study to suggest cut off value in LVGLS to inspect CAV in pediatric patients, according to our knowledge.

LVGLS is a well-established, sensitive marker of global longitudinal myocardial deformation. This parameter is based on semi-automatic myocardial deformation tracking in standard two-dimensional apical views and also direct angle measurements which are independent of loading and heart rate measurements of myocardial deformation. Also, it is a relatively easy to obtain measure and is considered to be highly robust with low interobserver and intraobserver variability.[7] Most importantly, it is non-invasive method which could broaden its applicability to pediatric patients. On this, in small children, myocardial strain analysis might be considered as the alternative method for evaluating the presence of CAV instead of invasive angiography including IVUS. Moreover, early detected deteriorated myocardial deformation might improve the outcome of heart transplantation.

Limitations

Our present study had some limitations of note. First, it was a single-center, retrospective study of pediatric Heart transplant patients who received transplants more than 1 year previously. Further studies are needed to clarify whether the use of invasive imaging can be postponed by a routine use of LVGLS in the monitoring of graft function and to evaluate the long-term prognostic

value of LVGLS.

Conclusion

The LVGLS, the parameter of longitudinal myocardial deformation is decreased significantly in children with CAV at one-year following a heart transplantation. Given the considerable technical limitations of conducting an angiographic diagnosis of CAV with/without IVUS in pediatric cardiac transplant recipients, LVGLS is the most valuable echocardiographic parameter for evaluating CAV in a non-invasive way and could therefore be the substantial viable alternative approach for CAV screening in children with heart transplant. Moreover, assessing this parameter may improve the outcomes of pediatric heart transplantation through an early diagnosis of CAV.

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Table 4. Pearson Correlation Analysis between CAV and Echocardiographic Parameters

Echocardiographic Parameters	Correlation coefficient (γ)	P value
LVEDD	- 0.084	0.56
LV mass index	0.05	0.73
LVEF	0.029	0.84
LVEDV	-0.008	0.96
LVGLS	0.648	0.08
LVGCS	-0.49	<0.01
LVGRS	0.184	0.35
RVGLS	0.134	0.52

Table 5. Area under the curve of Receiver operating curves according to Echocardiographic Parameters

Parameters	AUC	P value (95% CI)	Threshold	Sensitivity (%)	Specificity (%)
LV mass index	0.543	0.67 (0.33-0.76)	105.89	46.7	70
LVEF	0.467	0.74 (0.26-0.67)	66.87	60	50
LVGLS	0.800	<0.01 (0.65-0.95)	-14.03	73.3	80
LVGCS	0.373	0.21 (0.17-0.57)	-24.95	66.7	20
LVGRS	0.453	0.64 (0.25-0.65)	14.77	73.3	30
RVGLS	0.607	0.29 (0.42-0.80)	-8.39	73.3	50

배경: 심장 동종이식 혈관병증은 심장 이식 후의 주요 합병증으로 심이식을 시행한 소아 환자에서 후기사망률의 최고 25%를 야기하는 것으로 알려져 있다. 최근 speckle tracking echocardiography를 이용한 strain imaging 분석법이 심이식 환자에서의 심장 동종이식 혈관병증 스크리닝 방법으로 활용되고 있지만 이는 주로 성인 환자에게 국한되어 있다. 이에 본 연구는 소아 심이식 환자에서 심장 동종이식 혈관병증 스크리닝의 대체 방법으로서의 좌심실 심근 strain 분석법의 가능성을 평가해보고자 하였다.

연구방법: 본 연구는 1997년 8월부터 2017년 6월까지 서울아산병원에서 심장이식을 시행 받은 총 71명의 소아를 대상으로 하였다. 연구 대상자는 intravenous ultrasound (IVUS) 상에서의 심장 동종이식 혈관병증의 유무에 따라 두 그룹으로 분류되었고 IVUS 검사 상 관상동맥 내막의 두께가 0.5mm 초과인 경우 의미 있는 심장 동종이식 혈관병증이 발생한 것으로 정의하였다. 의미 있는 심장 동종이식 혈관병증이 발생한 군과 그렇지 않은 군에서의 이식 1년 후 시행한 심초음파 자료와 심도자술 결과를 비교 분석하였다.

결과: 좌심실 global longitudinal strain (LVGLS) 값이 심장 동종이식 혈관병증이 발생하지 않은 군에서 심장 동종이식 혈관병증이 발생한 군보다 의미 있게 높음이 확인되었다. (-15.8%±3.85% in the CAV(-) group vs -11.52%±3.78% in the CAV(+) group; p-value <0.01). 또한, ROC curve 분석을 통해 LVGLS 값이 -14.03% 보다 낮을 경우 73.3% 의 민감도와 80% 의 특이도를 가지고 심장 동종이식 혈

관병증 발생을 예측할 수 있음을 확인하였다.

결론: 본 연구를 통하여, 심장 이식 후 심장 동종이식 혈관병증이 발생한 소아에서 심근 변형의 저하가 확인되었다. 심초음파를 통한 심근 Strain 분석법은 관상동맥 혈관 조영술 시행이 제한되는 소아 심이식 환자에서 심장 동종이식 혈관병증 평가의 대안으로 고려될 수 있을 것이다.

Key words : 심장 이식, 소아 심장이식, 심장 동종이식 혈관병증, 심근 strain 분석