Effects of Pectus Excavatum Repair on Right and Left Ventricular Strain

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Background. The cardiopulmonary benefits of pectus excavatum repair have been debated. Echocardiographic speckle-tracking strain and strain rate have been used to evaluate and detect subclinical myocardial dysfunction in patients receiving cardiotoxic chemotherapy, and patients with valvular heart disease. This technology was applied to evaluate the effects of pectus excavatum surgery on left ventricular (LV) and right ventricular (RV) function.

Methods. Speckle tracing strain evaluation was performed on intraoperative transesophageal echocardiographic images acquired immediately before and after Nuss repair in adult patients (aged 18 years or more) from 2011 to 2014. Standard severity and compression indices were measured on chest imaging performed before pectus excavatum repair.

Results. In total, 165 patients with transesophageal echocardiographic images during repair were reviewed (71.5% male; mean age 33.0 years; range, 18 to 71; Haller index 5.7; range, 2.3 to 24.3). Significant improvement after repair was seen in global RV longitudinal strain (−13.5% ± 4.1% to −16.7% ± 4.4%, $p < 0.0001$) and strain rate (−1.3 ± 0.4 s^{-1} to −1.4 ± 0.4 s^{-1}, $p = 0.0102$); LV global circumferential strain (−18.7% ± 5.7% to −23.5% ± 5.8%, $p < 0.0001$) and strain rate (−1.5 ± 0.5 s^{-1} to −1.9 ± 0.8 s^{-1}, $p = 0.0003$); and LV radial strain (24.1% ± 13.5% to 31.1% ± 16.4%, $p = 0.0050$). There was a strong correlation between preoperative right atrial compression on transesophageal echocardiogram and improvement in RV global longitudinal strain rate immediately after pectus repair.

Conclusions. Mechanical compression and impaired RV and LV strain is improved by Nuss surgical repair of pectus deformity.

(Ann Thorac Surg 2018;105:294–301)

Pectus excavatum (PE) is a common malformation of the chest wall with posterior depression of the sternum and adjacent costal cartilages. That may cause physiologic symptoms and cardiopulmonary impairment with limitation of diastolic filling through mechanical compression of right-side heart chambers [1]. Beyond cosmetic considerations [2, 3], several reports have shown an improvement in pulmonary function [4–9] and exercise capacity [2, 3, 10–12] in PE patients after surgical repair. Transthoracic echocardiography studies have also demonstrated improvement in cardiac anatomy and function in patients with PE after surgical correction [2, 6, 10, 13–15]. We previously reported on improvement in left ventricular (LV) ejection fraction, increased right-side heart chamber size, and a 38% improvement in right ventricular (RV) cardiac output by intraoperative transesophageal echocardiography (TEE) [16] before and immediately after PE repair [17]. These improvements may be greater in older adult patients with a mean increase of more than 65% in cardiac output seen in patients over the age of 30 years [18].

No imaging study has evaluated the affects of mechanical compression on the right-sided cardiac chambers from PE and the benefits of cardiac decompression by PE surgery. Speckle tracking strain is a robust method that directly evaluates myocardial contractile function. It is not subject to the need for parallel alignment of the ultrasound beam with the area of interest or the tethering effects of surrounding segments as occurs with Doppler echocardiographic methods. In this retrospective observational study, we evaluated the effect of PE repair on RV and LV contractile function by two-dimensional speckle tracking strain in patients who underwent intraoperative TEE immediately before and after PE surgical repair.

Patients and Methods

A retrospective review was performed of all patients undergoing surgical correction of PE by a single surgeon and site using the techniques of modified Nuss [19] or

Accepted for publication Aug 7, 2017.

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Dr Jaroszewski discloses a financial relationship with Zimmer Biomet, Inc, and AtriCure, Inc.

Published by Elsevier Inc.

0003-4975/$36.00
http://dx.doi.org/10.1016/j.athoracsur.2017.08.017

Abbreviations and Acronyms

CT	= computed tomography
LV	= left ventricular
MRI	= magnetic resonance imaging
PE	= pectus excavatum
RA	= right atrium
RV	= right ventricular
RVGLSR	= right ventricular global longitudinal strain rate
TEE	= transesophageal echocardiography

hybrid (combined Nuss procedure with partial open cartilage excision/osteotomy, plating, and support bar placement) [20, 21] during the period of May 2011 to July 2014. The indications for surgical repair were based on thoracic anteroposterior compression indices: a Haller index from computed tomography (CT) or magnetic resonance imaging (MRI) imaging (inspiratory imaging and expiratory imaging when available) of 3.25 or greater [22], or correction index 20% or greater [23], or significant or progressing cardiopulmonary symptoms [24]. The study was approved by the Institutional Review Board.

Study Population

In total, 272 consecutive adult patients underwent a Nuss or hybrid Nuss PE repair during this period. Inclusion criteria for the study included repair of significant PE deformity (Haller index greater than 3.25 or evidence for cardiac compression). One hundred seven patients were excluded for the following reasons: (1) refusal to sign consent for study participation; (2) inadequate or technically poor TEE images available for retrospective review; and (3) prior open Ravitch procedure with extensive chest wall calcification and fusion or malunion with chronic pain. The final study population consisted of 165 patients with intraoperative TEE imaging performed immediately before and after PE repair. Information on blood pressure and heart rate was collected from anesthesia records as best estimated at the time TEE before and after surgery measurements were made. That was based on anesthesia recorded time of TEE probe insertion and end of surgery. A mean of three recorded times at both of these intervals was calculated. Computed tomography or MRI was available for review in 161 patients. A control group of 17 patients was studied to assess for changes on TEE that might be due to intraoperative variables including chest manipulation, general anesthesia, or changes in blood pressure or heart rate. This control group included patients with previous PE repair and placement of stainless steel pectus support bars who underwent planned staged pectus support bar removal with intraoperative TEE imaging before and after bar removal. No patients were receiving inotropes or vasoconstrictors during anesthesia.

Echocardiography

The TEE was performed using a multiplane X7-1 MHz transducer, coupled with a Philips I-E33 ultrasound machine (Philips Healthcare, Bothell, WA). The TEEs were performed by board-certified echocardiologists using the standard TEE image acquisition protocol from which select views, as shown in Table 1, were chosen for study-related data measurements. The frame rate of stored images was greater than 50 frames per second as per echocardiography laboratory practice at our institution for all echocardiography studies.

Echocardiography Image Analysis, RV and LV Strain Measurement

All intraoperative before and postoperative TEE images were evaluated. Digital Imaging and Communications in Medicine (DICOM) images stored at the time of TEE study were retrieved onto a ProSolv image viewer. Dedicated nonforeshortened preoperative and postoperative RV views in the mid esophageal plane view at 0 degrees were selected for measurement of RV strain and strain rate. Mid short-axis views of the LV in the deep gastric view before and after surgery were selected for measurement of LV circumferential strain. Selected DICOM images were uploaded from the ProSolv (Fujifilm Medical Systems, Stamford, CT) server onto a workstation with a commercial strain measurement software technology tool (Syngo US Workplace 3.5 with Velocity Vector Imaging [VVI]; Siemens Corporation, Malvern, PA).

The RV and LV strain and strain rate measurement was performed by a single observer (C.J.C.). Automatic tracing was based on placing of points of interest along the RV endocardial border (generally, 6 to 8 points in total) in end systole, starting from the lateral tricuspid annulus, covering the RV apex, and ending at the medial tricuspid annulus. Based on the points of interest, the software produces an automatic trace of the RV endocardium and epicardium, which can be edited by the user. The global strain was calculated from the average of the individual strain curves. When two or more segments were unavailable; the measurement was considered as suboptimal and was excluded. For LV strain measurement, LV endocardium was traced by placing points of interest (6 to 8 points in total) in the short-axis view at mid papillary muscle level (excluding the papillary muscles in the trace). This was followed by an automated trace of the entire epicardium and endocardium

Table 1. Transesophageal Echocardiography Imaging Protocol: Echocardiographic Evaluation of Cardiac Size and Function, and Imaging Angles

Cardiac Evaluation	Imaging
Right ventricle	ME, 0–10 degrees, four-chamber, RV focused
Right atrium	ME, 0–10 degrees, four-chamber, RA focused
Tricuspid annulus	ME, 0–10 degrees, RV focused
LV mid papillary short axis	Transgastric, 0–20 degrees

LV = left ventricle; ME = mid esophageal; RA = right atrium; RV = right ventricle.

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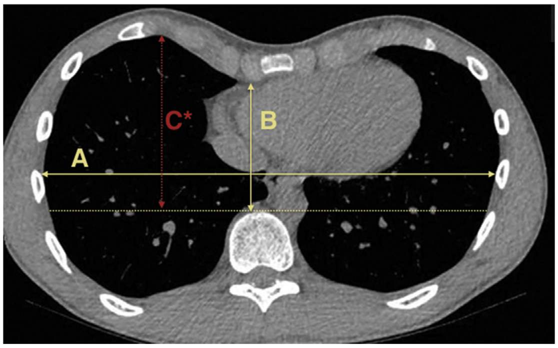

Fig 1. The definitions of computed tomography and magnetic resonance imaging (CT/MRI) indices and abbreviations are demonstrated on a computed tomography image. All measurements were performed in both inspiratory and expiratory phases: maximum transverse diameter (A), minimum anteroposterior dimension (B), maximum distance between a line placed on the anterior spine (dotted line), and the inner margin of the most anterior portion of the chest (C) [measured on the side with greater chest anteroposterior dimension, which is right side of chest in this figure]. Haller index = (A) divided by (B); correction index = (C) minus (B) divided by (C) times 100%.

throughout the cardiac cycle with the ability to edit any point along the trace. Global strain and strain rate are depicted on the screen once the user accepted the trace. Each strain value was the average of two or three measurements from separate cardiac cycles. All patients were in normal sinus rhythm, and all had normal LV and RV systolic function.

Table 2. Patient Hemodynamic and Baseline Transesophageal Echocardiography and Magnetic Resonance Imaging Data

Variables	Preoperative	Postoperative	p Value
Heart rate, beats/min	71.2 (12.9)	70.4 (12.4)	0.5525
Systolic blood pressure, mm Hg	106.1 (21.5)	122.0 (19.9)	<0.0001
TEE LVEF, %	60.4 (5.1)	…	…
Right atrium size, cm	3.34 (0.76)	3.84 (0.65)	<0.0001
Tricuspid annulus size, cm	2.45 (0.53)	2.71 (0.54)	<0.0001
RVOT size, end systolic, cm	1.62 (0.44)	1.71 (0.43)	0.1390
Expiratory minimum APD, mm	55.0 (14.9)	…	…

Heart rate and systolic blood pressure are expressed as median (SD), rest values are mean (SD).

APD = anteroposterior diameter; LVEF = left ventricular ejection fraction; RVOT = right ventricular outflow tract; TEE = transesophageal echocardiogram.

Interobserver Variability

Fifteen patients were randomly selected for repeat measurement of each strain parameter. Observer 2 was kept blind from the results measured by observer 1 before the final analysis.

Preoperative CT/MR Scans

The CT/MRI scans were performed preoperatively, and imaging was reviewed and available for 161 patients.

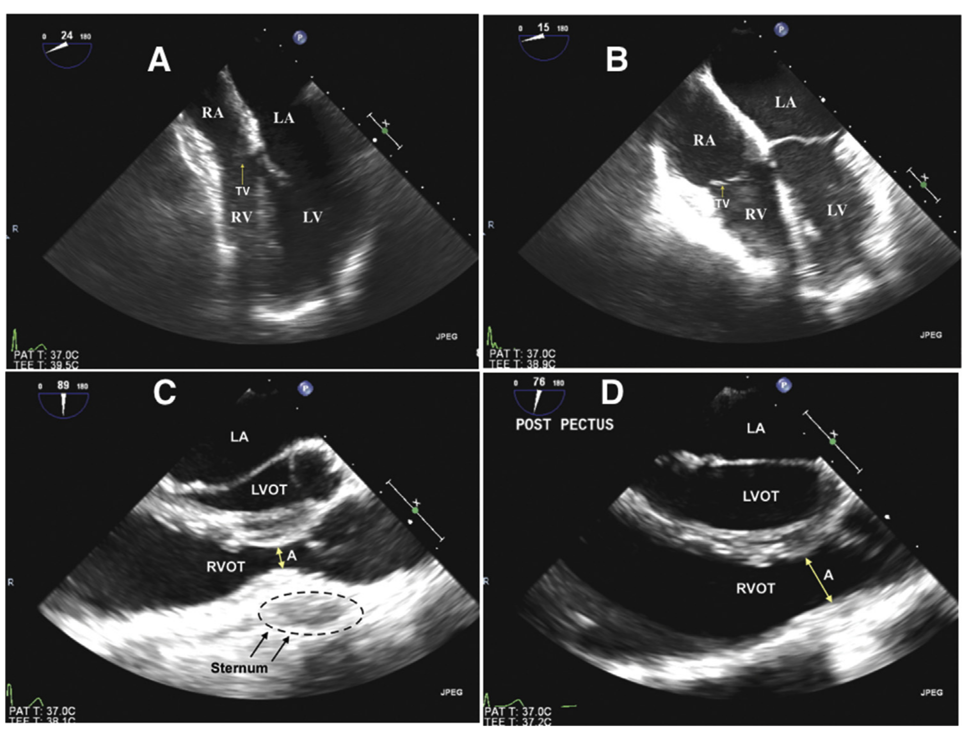

Fig 2. Transesophageal echocardiographic images demonstrating the effect of pectus repair surgery on right-side heart chamber size. (A) Mid esophageal, four-chamber view demonstrating compression of right atrium (RA), tricuspid valve annulus, and basal portion of right ventricle (RV) in end systole before Nuss pectus excavatum (PE) surgical repair. Prolapsing tricuspid valve (TV) is shown by yellow arrow. (B) Relief of RA, tricuspid annulus, and basal RV compression immediately after Nuss PE repair. Note the normal appearance of tricuspid valve (yellow arrow). (C) Mid esophageal views in end diastole demonstrating a narrow RV outflow tract (RVOT [yellow arrow labeled A, before surgery]), which (D) increased (yellow arrow labeled A) after surgery. Mechanical compression of the sternum on the RVOT is also demonstrated in (C), and as relieved by surgical repair (D). (LA = left atrium; LV = left ventricle; LVOT = left ventricular outflow tract.)

Inspiratory and expiratory diameters and indices were measured for both Haller index [22] and percent of correction index [25–27] by a single observer (M.G.) on preoperative CT/MRI scans, as described in Figure 1.

Statistical Data Analysis

Prism 5.0 (GraphPad Software, San Diego, CA) was used for statistical analysis. All continuous variables are expressed as mean ± SD, unless specified. The change of each parameter (delta) is defined as postoperative measurement minus preoperative measurement. A paired, two-tailed Student's *t* test was used for comparison between before and after surgery measurements for RV and LV strain and strain rate. Linear regression was used to analyze the correlations between all continuous variables. To assess reproducibility, the measurements of two observers were analyzed by paired, two-tailed Student's *t* tests. Bland-Altman plot and linear regression analysis were applied to analyze the consistency of interobserver measurements. A *p* value less than 0.05 was considered significant.

Results

In total, 272 patients underwent PE repair, of whom 165 met inclusion criteria and were evaluated. One hundred fifty-one patients (91.5%) were primary PE repair and 14 (9.5%) were revision of prior failed or recurrent PE repair. Mean age was 33.0 years (range, 18 to 71); 71.5% were male; mean Haller index was 5.7 ± 3.1 (range, 2.3 to 24.3) [22]. The 1 patient with Haller index of 2.3 was a revision of prior Nuss with dislodged bar. Mean age of the 17 patients in the control group was 35.2 years (range, 21 to 53), and 76.5% were male. For the control group, the average time between the first pectus repair surgery and the bar removal surgery was 3 years. Hemodynamic and echocardiographic data are reported in Table 2. Figure 2 shows changes observed in right atrial and ventricular chamber dimensions before and after PE repair in a representative patient.

Effect of PE Repair Surgery on RV and LV Strain and Strain Rate

Data on RV and LV strain measurements in 165 patients are shown in Table 3. All before and after repair comparisons, except LV radial strain rate, demonstrated significant improvement. In the control group, no significant changes in RV or LV strain were observed before and after surgical correction, as shown in Table 4.

Relationship Between Cardiac Compression and Changes in RV Size, RV Global Longitudinal Strain Rate, and Function After PE Repair

Expiratory imaging views were available preoperative in only 67 (41%) of the 165 patients. There was a strong relationship between TEE measured preoperative right atrial chamber size and both preoperative CT/MRI expiratory minimum anterior-posterior diameter and correction index. That correlated to a greater increase in postoperative right atrial size (Fig 3). Preoperative right-side heart compression of the right atrium (RA) on TEE

Table 3. Effect of Pectus Excavatum Surgery on Right Ventricular and Left Ventricular Strain

	Right Ventricular Strain Longitudinal				Left Ventricular Strain				Left Ventricular Strain Rate			
	Strain (%)		Strain Rate (s^{-1})		Circumferential (%)		Radial (%)		Circumferential (s^{-1})		Radial (s^{-1})	
(n = 168)	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Mean (SD)	−13.5 (4.1)	−16.7 (4.4)	−1.3 (0.4)	−1.4 (0.4)	−18.7 (5.7)	−23.5 (5.8)	24.1 (13.5)	31.1 (16.4)	−1.5 (0.5)	−1.9 (0.8)	1.9 (1.3)	2.0 (0.9)
p Value	<0.0001		0.0102		<0.0001		0.0050		0.0003		0.3230	

The more negative the value, the better the longitudinal strain and strain rate; the more positive value, the better the radial strain. Reference range of transthoracic echocardiography measured strain in adults with no cardiovascular disease: right ventricular (RV) global longitudinal strain −20.4% ± 3.2%; RV global longitudinal strain rate −1.2 ± 0.2 s^{-1}; left ventricular (LV) circumferential strain −21.9% ± 4.0%; LV radial strain 44.8 ± 21.7%; LV circumferential strain rate −1.3 ± 0.3 s^{-1}; LV radial strain rate 2.3 ± 0.7 s^{-1} [36]. We previously reported, within the same cohort, the improvement in right atrial, tricuspid annulus end-systolic, right ventricular outflow tract end-diastolic, and end-systolic dimension was 15.1%, 10.9%, 6.1%, and 6.1%, respectively [17].

Post = postoperative; Pre = preoperative.

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Table 4. Effect of Bar Removal on Right Ventricular and Left Ventricular Strain, Control Subjects

	Right Ventricular Strain Longitudinal				Left Ventricular Strain				Left Ventricular Strain Rate			
	Strain (%)		Strain Rate (s^{-1})		Circumferential (%)		Radial (%)		Circumferential (s^{-1})		Radial (s^{-1})	
(n = 17)	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Mean (SD)	−13.4 (3.1)	−12.3 (4.6)	−1.1 (0.4)	−1.0 (0.3)	−19.3 (6.6)	−19.0 (2.4)	31.0 (21.3)	23.8 (12.4)	−1.4 (0.4)	−1.4 (0.3)	2.2 (1.3)	1.7 (0.5)
p Value	0.9756		0.6084		0.6807		0.7140		0.2362		0.3301	

The more negative the value, the better the longitudinal strain and strain rate; the more positive value, the better the radial strain. Reference range of transthoracic echocardiography measured strain in adults with no cardiovascular disease: right ventricular (RV) global longitudinal strain −20.4% ± 3.2%; RV global longitudinal strain rate −1.2 ± 0.2 s^{-1}; left ventricular (LV) circumferential strain −21.9% ± 4.0%; LV radial strain 44.8 ± 21.7%; LV circumferential strain rate −1.3 ± 0.3 s^{-1}; LV radial strain rate 2.3 ± 0.7 s^{-1} [28].

Post = postoperative; Pre = preoperative.

also correlated with improvement in RV global longitudinal strain rate (RVGLSR) after PE repair surgery. There was a positive correlation between preoperative RVGLSR and an improvement in it after surgery (Fig 4). We did not find significant correlation between inspiratory imaging (including Haller index) and RVGLSR.

Interobserver Reproducibility

The mean preoperative RVGLSR (n = 10) values were -1.2 ± 0.2 s^{-1}, and -1.2 ± 0.2 s^{-1}, for observer 1 and observer 2, respectively ($p = 0.1531$). Linear regression showed strong linear correlation ($r = 0.90$, $p < 0.0001$) between the two observers. Bland-Altman analysis revealed close agreement between the two observers with a mean bias of −0.045.

Comment

Mechanical Compression of Heart and Effects on Myocardial Strain

Strain and strain rate measurements on speckle-tracking images have been widely used to detect subclinical myocardial dysfunction [18, 27–30]. Only a few studies, however, have evaluated myocardial strain in conditions that produce cardiac compromise due to direct mechanical compression, such as cardiac tamponade [31] and constrictive pericarditis [30]. Aksakal and associates [31] demonstrated improvement in strain in the basal lateral LV segments after pericardiocentesis in patients with cardiac tamponade. Their findings suggest that mechanical compression may cause reduced myocardial strain, and that this can be relieved with removal of mechanical compression. Two additional studies used strain analysis to differentiate constrictive pericarditis and restrictive cardiomyopathy [30, 32]. Their results further indicated a reversible impairment in myocardial strain caused by mechanical compression. When compared with control subjects and patients with restrictive cardiomyopathy, patients with constriction showed more severe reduction in LV regional strain, RV free wall longitudinal strain [30], and LV circumferential strain [32]. Kusnose and associates [30] in their study further showed that pericardiectomy improves LV global longitudinal and circumferential strain and the ratio of LV anterolateral strain to LV septal strain.

The chest wall deformity of PE causes mechanical compression of the heart, which can be corrected by surgical intervention [19]. We have previously demonstrated that surgical repair of PE deformity results in a significant increase in RA and basal RV chamber size and a corresponding increase in RV stroke volume and cardiac output [17]. Improvements seen after surgery in RV preload, stroke volume, and cardiac output could be partially related to an intrinsic improvement in RV strain and strain rate. Similar to the observations of Kusunose and colleagues [30], we found an improvement in LV circumferential strain and strain rate after PE repair in our cohort. An improvement in LV strain did not, however, correlate with the severity of chest deformity (as determined by the

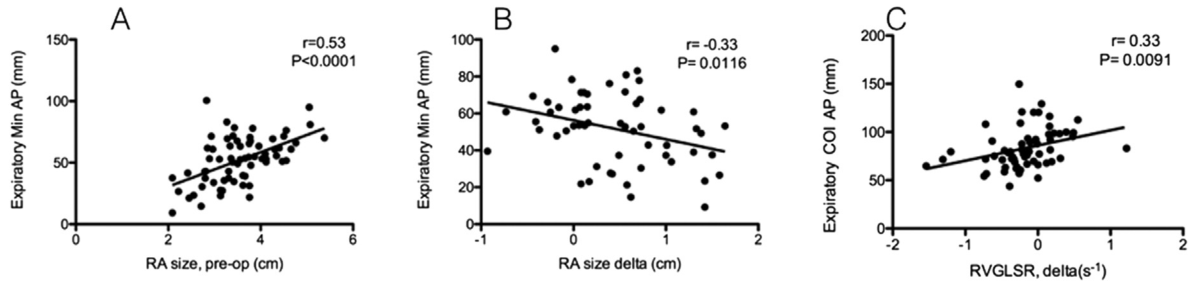

Fig 3. Linear correlations of computed tomography (CT) and magnetic resonance imaging (MRI) cardiac compression indices and right heart chamber size/strain measurements. There was a strong correlation between (A) expiratory CT/MRI minimum (min) chest anterior-posterior (AP) diameter and preoperative (pre-op) right atrium (RA) size; (B) minimum chest AP diameter and improvement in RA size after surgery; and (C) correction index (COI) AP with the improvement of right ventricle global longitudinal strain rate (RVGLSR).

Haller index) or the change in RA size. The anterior location of the RV, thin wall and low pressure subject the RV to the direct mechanical compression in patients with PE deformity. Relief of RV sternal compression may cause improvements in RV preload [33], with subsequent increase in cardiac output. In the study group, the preoperative and postoperative median heart rates were not significantly different (71.2 ± 12.9 beats/min versus 70.4 ± 12.4 beats/min, $p = 0.5525$). The systolic blood pressure measurements in the study patients postoperatively were significantly higher than the preoperative status (106.1 ± 21.5 mm Hg versus 122.0 ± 19.9 mm Hg, $p < 0.0001$). The difference in blood pressure can be explained by recent induction anesthesia without surgical stimulus at time of probe insertion and lighter anesthesia at the completion of the surgical procedure. Notwithstanding the impact of anesthesia, a higher postoperative blood pressure would favor our data. An increase in afterload should cause a worsening of LV strain, unlike our findings of improvement in LV strain after PE surgery.

Controversy Regarding Cardiopulmonary Benefit of PE Correction

The cardiopulmonary implications and benefits of surgical correction in PE have been debated, with studies reporting both positive [2–5, 10, 11, 13] and nonsignificant effects [6–9, 12, 34] of pectus repair surgery. From a physiologic standpoint, relief of significant cardiopulmonary compression by PE surgery should increase the anterior-posterior thoracic dimension and facilitate cardiac filling and an improvement in exercise capacity [2]. Regardless of the timing of postoperative echocardiographic assessment, studies that used transthoracic echocardiography or TEE have reported an improvement in structural or functional parameters, including left [2], right [10], or bilateral [16] ventricular dimensions, stroke volume [6, 13–15], LV ejection fraction [16], and cardiac output [6, 14, 15] after repair. Another recent cardiac MRI study also revealed a significant improvement in both RV and LV ejection fraction 1 year after surgery [35]. In our patient cohort, intraoperative TEE performed in patients after Nuss surgical PE repair demonstrated an immediate improvement in RV and LV contractile function by speckle tracking strain.

Study Limitations

This study is inherently limited by its retrospective nature. A large number of patients with incomplete echocardiography images or who refused study consent were excluded, and a bias may have been introduced. Global strain was calculated from the average of the individual strain curves. When two or more segments were unavailable, the measurement was considered as suboptimal and the patient was excluded. In the excluded group,

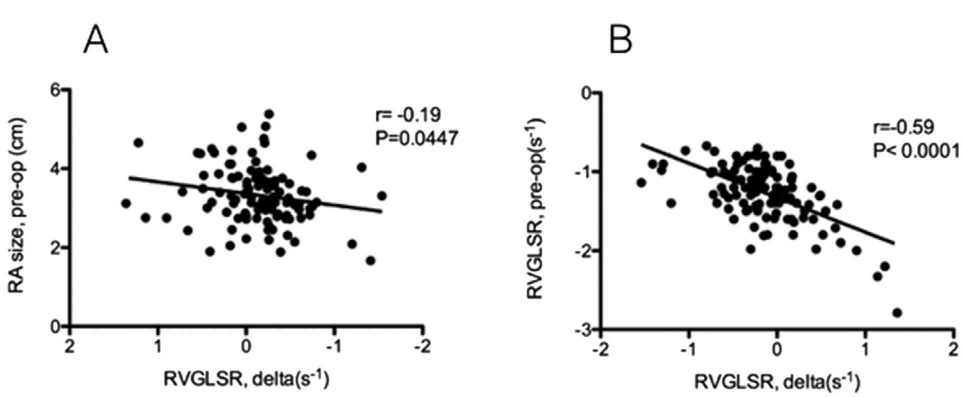

Fig 4. Preoperative (A) right atrium (RA) size and (B) right ventricle global longitudinal strain rate (RVGLSR) correlated with an improvement in RVGLSR after pectus excavatum repair surgery. Note that right ventricle strain and strain rate are negative values, and more negative values of strain and strain rate indicate better contractile function. That also gives a negative correlation coefficient and indicates the more impairment of strain rate at baseline gives a greater improvement of strain function. (pre-op = preoperative.)

median age was not significantly different; however, there were fewer men (53% versus 71%). Severity by Haller index of the excluded group was also significantly less when compared with the included group (Haller index 3.6 $\pm$ 0.8 versus 5.7 $\pm$ 3.1, $p < 0.0001$). There was an observed tendency for patients who were less symptomatic and more cosmetic oriented to refuse study consent. Imaging performed by the cardiologist also tended to be less detailed in patients who had predominantly cosmetic issues.

The respiratory cycle may influence cardiac chamber dimension; however, care was taken to perform measurements during suspended end expiration. The reader was not blinded to before versus after repair images (which were annotated on the screen). Changes in hemodynamic conditions before and after surgery may influence chamber dimensions as well as cardiac output. We did not perform measurement of LV longitudinal strain and strain rate owing to the difficulty of obtaining axis longitudinal LV views with PE deformity.

Conclusion

Direct mechanical compression in patients with PE causes impairment and RV and LV strain. Immediate measurable improvement in RV and LV strain was seen after Nuss PE repair. Further studies are being pursued to assess whether this improvement in cardiac strain translates into a demonstrable increase in exercise capacity.

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