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Research progress in the effects of pectus excavatum on cardiac functions

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ABSTRACT

Background Pectus excavatum, the most common chest wall deformity in children, accounts for nearly 90% of congenital malformations of chest wall. Initially, both parents and doctors paid more attention to the influence of this deformity on patient appearance and psychology. Following deeper studies of pectus excavatum, researchers found that it also affected cardiac functions. The purpose of this review aims to present recent research progress in the effects of pectus excavatum on cardiac functions.
Data sources Based on aspects of CT, ultrasound cardiography (UCG) and MRI, all the recent literatures on the influence of pectus excavatum on cardiac function were searched and reviewed.
Results Moderate and severe pectus excavatum did have a negative effect on cardiac function. Cardiac rotation angle, cardiac compression index, right atrial and tricuspid annulus size, septal motion and myocardial strain are relatively effective indexes to evaluate cardiac function.
Conclusions Pectus excavatum did have a negative effect on cardiac function; so surgeons should actively diagnose and treat such patients in clinical work. However, further research is needed on to explore the measures and indicators that can reflect the changes of cardiac function in patients objectively, accurately, effectively and timely.

INTRODUCTION

Pectus excavatum (PE) accounts for 90% of congenital chest wall malformations. One in every 400–1000 newborns has PE with a 3–5:1 male to female ratio. It is characterized by a ‘navicular’ or ‘funnel’ shaped depression of partial sternum, costal cartilage and ribs into the thoracic cavity. The deepest depression is generally located at the junction of sternum body and xiphoid.[1–4] The deformed chest wall compresses the thorax and its contents. Heart and lungs are coupled systems, and the effect on one will influence the other. Perhaps for this reason, there is no consensus on the effect of PE on cardiac functions of patients.[5–9]

Thoracic morphological changes with impaired cardiac functions

Effects of chest growth and development on cardiac functions

The development of the thorax is similar to the physical growth and development of children, growing in a gradual but not completely linear manner. Chest wall compliance among infants and young children is relatively better and can completely compensate for the impaired cardiac function; therefore, PE progresses slowly with about 22% of cases being noticed before the age of 10.[10] As children age, their chest wall compliance elasticity and flexibility gradually decrease, leading to clinical symptoms of impaired cardiac function, such as decreased exercise endurance, breathing difficulties, chest pain, and so on. Sarwar *et al*[2] and Lollert *et al*[3] found that clinical symptom aggravation of children mainly occurred in adolescence. With the second growth peak (adolescence coming), development of the thoracic cavity changed sharply, leading to increasingly aggravating clinical symptoms.

Effects of changes in heart anatomical morphology on cardiac functions

The anatomical changes of right ventricle (RV) morphology in some children with PE will affect cardiac function, and the disorder of cardiopulmonary function will cause clinical symptoms.[11–13] Humphries *et al*[14] believed that the main cause of exercise intolerance was heart compression rather than lung limitation. PE is characterized by a reduction in anterior-posterior diameter of the thorax associated with ventricular displacement and rotation, resulting in ventricular compression. In severe cases of PE, the sternal depression may lead to distortion of the cardiac chambers and great vessels,[15] mitral valve prolapse (MVP) and other cardiac dysfunction.[10 16] With consistent compression of right heart chamber by deformed chest wall, children with PE would suffer morphology changes and decreased cardiac function.[8 15 17–20] Chan Wah Hak *et al*[21] thought children's symptoms were caused by severe stress on the RV, and in 2014 Chan Wah Hak *et al* reported one case with a rare ECG abnormality caused by RV compression. This case was examined using echocardiography (UCG) and MRI. Preoperative UCG showed hypokinesia and thinning of the right ventricular inferior wall, no tricuspid valve prolapse or regurgitation. Preoperative cardiac MRI revealed that there was severe displacement and compression of the RV, thinning and hypokinesia of the wall, and ejection fraction (EF) decreasing. After relieving cardiac compression by Nuss procedure, UCG revealed that RV size and systolic function had returned to normal. There was no abnormal cardiac structure 3 years after surgery. However, Oezcan *et al*[20] believed that the impact of chest wall malformations on cardiac anatomy and function included RV compression, and compression of the left atrium (LA). Humphries *et al*[14] considered that the reduction of anterior-posterior diameter of the thorax compressed the RV and the LA because they were located in the midline and were sandwiched between the concave chest wall and the spine; thus, these two chambers were mainly involved. However, bone limitation caused by the anterior chest wall depression essentially kept the diastolic blood pressure of the two cardiac chambers fixed. In addition, the right atrium also may be involved.

Progress in detecting impact of PEpectus excavatum on cardiac functions using imaging modalities

The severity of PE malformation determines its impact on cardiopulmonary function.[22] Depression of the sternum leads to a decrease in thoracic volume, which results in compression of the heart, lungs and adjacent tissues, affecting respiratory and circulatory functions.[23] Therefore, MRI, CT and UCG are very important imaging techniques for detecting the anatomical changes of thorax and heart in children with PE.

CT scanning

A CT scan can directly show the morphological changes of bony thorax of PE. Accurate measurement of Haller index (HI) can help understand the pulmonary lesions, sternal depression degree, heart location, intraoperative precautions and postoperative improvement.[24] Before surgery, multi-slice spiral CT can be used to make a comprehensive and accurate judgment on the degree of thoracic deformity and cardiopulmonary compression.[25] However, it is believed that the compression shown on CT images may not be significantly related to clinical symptoms.[14]

Chu *et al*[26] performed chest CT scans on 63 patients with PE who underwent surgical correction, measuring the depth of sternal depression, CT compression index, cardiac rotation angle, and pulmonary vein angle of each patient. Analysis of these data revealed that the mean sternal depression in these children was 21±7 mm and that compression occurred in all four chambers. The CT compression index was bounded by 2.4. Patients with index less than 2.4 had a smaller rotation angle than those whose index ranged from 2.4 to 2.9 or exceeded 2.9. The relationship between pulmonary vein angle and CT compression index was opposite. Chu *et al*[26] revealed that increases in CT compression index coincided with increases in cardiac rotation angle (correlation coefficient=0.75). Zhang *et al*[27] retrospectively analyzed the original CT images of 44 children with thoracic deformity, including 25 cases with PE (7 mild, 5 moderate, and 13 severe cases), and found that the depression degree of thorax was positively related to rotation angle of the heart.

Huang[24] performed preoperative and postoperative chest CT scans and calculated HI and cardiac rotation angle on 70 children with PE admitted from November 2015 to July 2017. The results revealed statistically significant differences in HI and cardiac rotation angle before and after surgery. Moreover, the increases in HI coincided with increases in rotation angle of the heart. Xie *et al*[28] divided 73 children with PE into two groups. Thirty cases received both routine dose and low-dose chest CT scan before Nuss procedure, and no statistical difference of the measured HI and cardiac rotation angle in patients was found between two different scanning methods. Low-dose chest CT scans were performed in the remaining 43 and 56 cases who were followed up for 6–12 months after Nuss procedure, with measurement of the HI and heart rotation angle to evaluate the degree of thoracic deformity and to analyze the influence of sternal depression on the shape and position of the heart. The results showed that the difference of HI and cardiac rotation angle between the moderate and severe PE groups was statistically significant and a high positive correlation between HI and cardiac rotation angle was also found. In the study of Xie *et al*, the results indicated that the degree of thoracic indentation increased the more the heart was displaced and the more the heart rotated to the left.

Echocardiography

Changes in cardiac function caused by compression in heart anatomical morphology by PE are normally detected by UCG, such as MVP, septum abnormalities, compression of RV and right ventricular outflow tract obstruction.[16 29–31] UCG has little effect on children, is easy to perform, and allows the structure and changes of each chamber and valve to be observed. However, a disadvantage is that UCG is easily influenced by RV structure, retrosternal position, and motion complexity.[32]

In 2016, Maagaard and Heiberg[33] searched three databases from 1972 to 2016 and 21 published studies that contained complete data were included, in which UCG data were compared before and after PE procedure to investigate cardiac function during rest and exercise. Among these included studies, Chao *et al*[34] and Sigalet *et al*[35] showed an increase in postoperative right ventricular output. Among six studies on EF, only Krueger *et al*[36] showed an immediate increase in EF after surgery with statistical significance. The researcher suggested that EF might have been underestimated preoperatively due to the influence of three-dimensional ventricular structure in the case of large SD. Maagaard and Heiberg[33] thought that generally the EF did not change following surgery. Lesbo *et al*[37] revealed that the compression of the deformed sternum on the heart would reduce the end-diastolic volume, and thus affect the cardiac output and EF and reduce the endurance of children.

In 2013, Maagaard *et al*[8] measured HI in 75 adolescents (49 patients and 26 controls) before surgery and at 1 and 3 years postoperatively (after pectus bar removal) during rest and exercise, respectively. Cardiac output, heart rate, and aerobic exercise capacity were measured by a photoacoustic gas-rebreathing technique. UCG was used to exclude potential mitral valve regurgitation and other possible structural abnormalities, and to examine the maximum cardiac index, fractional shortening (FS), EF, left ventricular diameter (LVD) and right ventricular diameter (RVD). During the preoperative exercise, the results showed the maximal cardiac index of the children was lower than that of the control group, and the value increased significantly at 1 and 3 years after the procedure, and no difference was observed between the case group and the control group. However, no correlations were observed between preoperative and postoperative HI and maximal cardiac index. In addition, no differences in EF, FS, LVD or RVD were observed between the case group and the control group.

In 2016, Sun *et al*[38] used CT to measure HI, cardiac compression index (CCI) and cardiac rotation angle at the most obvious level of sternal depression in 51 children with PE. UCG was performed simultaneously to measure LVD, RVD and left ventricular ejection fraction (LVEF). The results showed that with the exception of LVEF the differences between preoperative and postoperative parameters detected by CT and UCG were statistically significant, and the changes in preoperative and postoperative heart compression index and LVD were positively correlated with HI, with the heart compression index being the best postoperative improvement value.

Chao *et al*[34] conducted a retrospective study of 17 patients who received preoperative and postoperative transesophageal echocardiography (TEE) between 2011 and 2014. They calculated and recorded right atrial (RA) size, tricuspid annulus size, right ventricular outflow tract size, RV stroke volume, and RV output. The results showed that the right heart chambers size increased significantly after operation. Postoperative RA, end-systolic tricuspid annulus, end-diastolic RV outflow tract, end-systolic RV inner diameter, stroke volume and RV output all increased compared with their preoperative levels, while heart rate and systolic blood pressure showed no significant changes. Preoperative HI was not significantly correlated with RV stroke volume or RV output, but RV stroke volume was significantly correlated with RA size and tricuspid annulus size. Inclusion, the assessment of right cardiac function through preoperative RA and the tricuspid annulus size measured by TEE were better than that through HI.

Recent studies of de Siqueira *et al*[39] and Smiseth *et al*[40] have shown that myocardial strain can be used as a highly sensitive indicator of ventricular function rather than EF because changes in myocardial strain occur prior to EF decline. In 2018, Chao *et al*[41] studied the strain of left ventricle (LV) and RV during PE repair. A total of 165 children from 2011 to 2014 underwent preoperative and postoperative TEE examination. Strain and strain rate were measured by specific software, and standard severity and compression indices were computed from chest imaging that was performed before PE surgery. The RV longitudinal strain and strain rate, the LV global circumferential strain and strain rate, and the LV radial strain increased significantly after surgery. The preoperative RA compression and improvement in RV global longitudinal strain rate were strongly correlated, and there was a strong relationship between preoperative RA size and both preoperative expiratory minimum anterior-posterior diameter and correction index (CI), which may be related to an increase in RA size after surgery; however, the RV longitudinal strain rate was not correlated with the HI in the inspiratory image. A comparison of the two TEE studies published by Chao *et al*[34,41] in 2015 and 2018 revealed that PE repair can increase the size of right chambers, the stroke volume and the output. In addition, the increase of postoperative RV preload, stroke volume and cardiac output may be related to the improvement of RV strain and strain rate. This was similar to the results of Kusunose *et al*.[42] Chao *et al*[41] also found that LV circumference strain and strain rate increased postoperatively, while improvement of LV strain was not correlated with severity assessment of chest wall malformation (HI) or with change of RA size.

Nomura *et al*[43] recently demonstrated that compared with normal controls, patients with PE had characteristic changes of the shorter posterior mitral leaflet, the longer anterior mitral leaflet, the shorter coaptation depth, and the longer papillary muscle tethering length. The authors concluded that the continuous mechanical stress would promote degeneration, shrink leaflet gradually, and would cause mitral prolapse and significant regurgitation as well. This finding may provide an early clue to the etiology of MVP in PE.

MRI

As a widely used technique at present, MRI plays an important role in evaluations of PE. Because MRI characterizes myocardial changes in various diseases, it has become the gold standard for assessing cardiac function in all cardiovascular diseases. Furthermore, the radiation dose requirements in auxiliary examinations make cardiac MRI even more important in evaluations of PE.[29] Although MRI is used as the gold standard for evaluating cardiac function in all cardiovascular diseases, its application in children with PE has not been studied until recently.[1,14–16]

Humphries *et al*[14] used MRI to measure the end-diastolic and end-systolic volume, wall thickness, myocardium index, stroke index, and partial and total left and right ventricular function of six children with clinical symptoms of PE before surgery and 6 weeks after surgery. Preoperative MRI results showed that there were signs of compression in the anatomical morphology and hemodynamics of the hearts of all enrolled children, and the degree of anterior-posterior diameter stenosis of the thorax was significantly improved after surgery. The average HI decreased from 5.0 to 3.2 before and after surgery, respectively. Postoperatively, cardiac function was improved in all the children: RV compression was completely relieved in five cases, mild residual RV compression in one case, five cases of mild LA compression, and one case of moderate LA compression. Of four patients who experienced tricuspid regurgitation preoperatively, two were significantly improved without residual regurgitation after surgery. The study revealed that PE affected cardiac function through compression of heart chambers and that surgery can relieve the pressure on the heart and improve heart function.

Töpper *et al*[16] performed MRI examination on 38 children with PE before and after surgery to evaluate chest wall morphology, chest wall asymmetry index (AI), cardiac deformity indexes, CCI, cardiac asymmetry index (CAI), cardiac left lateral shift (CLLSH), right ventricular ejection fraction (RVEF), LVEF, LVD, RVD, and so on. These examinations found that RVEF was lower than normal before surgery and that RVEF significantly increased 1 year after surgery compared with the preoperative level. LVEF was within the normal range before surgery, and follow-up 1 year after surgery showed further improvement. CCI and CAI improved immediately after surgery, and the results remained stable until the last follow-up (postoperative follow-up (472±162 days)). In this study, it was proved that the effect of PE on cardiac function was mainly manifested by decreased RVEF and that surgery could significantly relieve right ventricular compression, which was consistent with the findings of Humphries *et al*.[14] In addition, CLLSH was improved at the postoperative (120±47 days) follow-up and was significantly improved at the last follow-up.

Deviggiano *et al*[13] were the first to study the relationship between PE indexes and 'cardiac anatomy and function' during breathing. A total of 62 children with PE underwent MRI and CT examination during expiration and inspiration, and the results showed that RV short diameter and LV eccentric index were significantly higher during inspiration than that during expiration, which was associated with a significant increase in LV diameter during inspiration. HI, CI and AI were higher in children with pericardial effusion than in those without pericardial effusion. The patients with a relative septal excursion equal to or larger than 11.8% were more severe than those with the excursion of less than 11.8%, and the relative septal excursion was positively correlated with HI, CI and AI. LV eccentricity index was weakly correlated with HI, CI and AI. The tricuspid annulus size was negatively correlated with HI, CI and AI. Left atrial and RA areas were negatively correlated with HI, CI and AI as well. The study showed that the dimensions of heart chambers and cardiac function changed significantly during the respiratory cycle, indicating that the changes in heart anatomy, morphology and function were related to the severity of PE, which was manifested as an exaggerated interventricular dependence shown by the respiratory-related septal excursion and the markedly increased LV eccentricity index particularly. In addition, PE severity was also inversely related to the width of tricuspid annulus size and LA area.

In 2017, Dore *et al*[29] performed chest X-ray and UCG on all patients since 2015. Patients with severe symptoms of PE (HI >3.2) underwent both inspiratory and expiratory MRI simultaneously. The evaluated relationship between PE indexes (HI, CI, AI, and so on) and cardiac function (LVEF, RVEF) has revealed that there were significant differences in HI and CI between inspiration and expiration in 20 subjects. Preoperative echocardiography showed normal RVEF and LVEF, while cardiac MRI disclosed an RVEF of 50.3%, with 18 of the 20 patients under the normal threshold of 61%, indicating that UCG underestimated the effect of PE on cardiac function.

Myocardial strain is a new research direction in the study of cardiac function. In 2017, Truong *et al*[32] performed MRI on 50 cases with PE and 20 healthy subjects to measure the size and function of the heart and to evaluate myocardial strain. Compared with healthy subjects, the mid-cavity circumferential strain magnitude of the cases was significantly decreased and the apical circumferential strain and the basal circumferential strain were significantly increased. No significant differences were observed in right ventricular global longitudinal strain, LVEF and RVEF. It was suggested that mid-cavity circumferential strain magnitude significantly decreased in patient group may be explained by geometric distortion of the RV due to sternal compression in PE and that basal circumferential strain as well as apical circumferential strain was increased as compensatory mechanisms for reduced mid-cavity circumferential strain. Töpper *et al*[16] conducted preoperative and postoperative cardiac MRI in 38 children and found that preoperative RVEF was significantly decreased and improved after surgery. In contrast, Truong *et al*[32] showed no difference in RVEF before and after surgical correction, which might attributed to severity of PE. Saleh *et al*[44] performed cardiac MRI study on 30 children with PE and found that RVEF was reduced, short dimension of RV was decreased both at end diastole and end systole, and RV long dimension was increased at end diastole. Lollert *et al*[45] conducted a preliminary study on the evaluation of myocardial strain differences by MRI in 14 PE cases and 14 healthy controls and found that RVEF was slightly decreased in five of the PE cases. Compared with healthy subjects, the children with PE had a significantly higher left ventricular longitudinal strain, mid and apical circumferential strain as well as apical circumferential strain rate, mid right ventricular circumferential strain and strain rate, and apical right ventricular circumferential strain and strain rate. No significant differences in right ventricular longitudinal strain and strain rate were observed between patients with PE and healthy subjects.

Capunay *et al*[46] studied the correlation among sternal torsion, cardiac compression and chest malformation in 116 patients with PE by cardiac MRI and CT. In this study, sternal torsion was independent of age, right-sided (clockwise) sternal torsion was more frequent and more severe than left-sided torsion, right-sided sternal torsion was significantly related to the cardiac compression classification, and the tricuspid/mitral annulus width ratio was significantly lower. Therefore, a significant inverse relationship between sternal torsion degrees and the tricuspid/mitral ratio also was demonstrated.

Rodriguez-Granillo *et al*[47] performed a study on 59 patients with PE and 20 healthy volunteers with no chest wall deformity using multimodality imaging to assess the impact of PE on cardiac morphology and function according to the site of maximum compression. All patients underwent CT, cardiac MRI and UCG to be evaluated of diastolic function and trans-tricuspid gradient during stress and systolic function and respiratory-related septal wall motion abnormalities. Peak exercise capacity in patients with PE was significantly lower than that in the control group and significant differences were found in left ventricular E/A and e/a ratio, right ventricular E/A ratio and trans-tricuspid gradient between groups at stress. Septal motion abnormalities were significantly correlated with the cardiac compression classification. Patients with PE, especially those with compression deformities affecting the RV and atrioventricular groove, exhibited multiple cardiac abnormalities that were associated with exertion, inspiration, and diastolic function.

CONCLUSIONS

To sum up, PE is the most common chest wall deformity. Multiple studies have evaluated the thoracic index, exercise capacity, cardiac anatomical morphology, EF, diastolic function, septal motion, cardiac rotation angle, inner diameter of cardiac chamber, myocardial strain, sternal torsion and cardiac compression in patients with PE by CT, UCG, and MRI to analyze the negative effect of moderate and severe PE on cardiac functions. Cardiac rotation angle, CCI, RA and tricuspid annulus size, septal motion and myocardial strain are relatively effective indexes to evaluate cardiac function, but there is no consensus on which of these measures is more objective and accurate, so further research is needed.

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