Applications of the Myocardial Strain Study using Two-Dimensional Speckle Tracking in Pediatrics

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Introduction

Myocardial strain has proved to be a useful tool in the evaluation of diastolic and systolic function, both in adults and in the pediatric population.[1] The study of myocardial strain by speckle tracking is a method independent from the angle of insonation and presents low intra- and interobserver variation, which allows to quantify global and regional ventricular function more accurately than traditional methods, such as tissue Doppler, shortening or ejection fraction.[2] This technique allows the evaluation of myocardial strain in the longitudinal, circumferential and radial axes, besides estimating ventricular rotation and torsion. Recent studies have also investigated atrial strain, which contributed to a better understanding of the pathophysiology of heart failure with preserved ejection fraction (HFpEF).

Some studies have demonstrated a high prognostic value of the strain obtained by speckle tracking, emphasizing its usefulness in both congenital and acquired pathologies.[3] However, myocardial strain is subject to physiological variations caused by age, sex, heart rate, preload, blood pressure and body surface, in addition to the type of software used for analysis.[4] Continuous efforts have been made to establish normal strain values that can be used as a universal reference in pediatrics, so that the assessment of myocardial strain be incorporated into the guidelines and be adopted in the clinical routine.[5-7] For now, the study of myocardial strain in the various pediatric pathologies falls in Degree of Recommendation II and Level of Evidence B.

This review describes the main applications of strain by two-dimensional speckle tracking in pediatrics.

Ventricular strain in heart diseases acquired in childhood

The evaluation of right and left ventricular strain is particularly useful in situations in which subclinical systolic and/or diastolic dysfunction is to be identified. The information obtained from the strain analysis allows for timely therapeutic intervention in several systemic diseases that include myocardial involvement.

Keywords

Heart Defects, Congenital/physiopathology; Child; Cardiomyopathy, Dilated; Cardiotoxicity; Stroke Volume; Echocardiography/methods; Echocardiography, Doppler; Image Interpretation, Computer-Assisted.

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Early detection of myocardial injury secondary to the use of anthracyclics is one of the most relevant contributions of the myocardial strain study to date and has been incorporated into follow-up protocols for cancer patients. There is consensus that a reduction of more than 15% in left ventricular (LV) global peak systolic longitudinal strain on pre-chemotherapy tests is a sign of cardiotoxicity in adults, even if the ejection fraction remains within the normal limits and there are no clinical signs of heart failure (HF).[8] Reduction of strain in these asymptomatic patients can predict a subsequent decrease in ejection fraction and/or future evolution to HF, with 65-85% sensitivity and 73-95% specificity according to a recent systematic review.[9] SUCCOUR (Strain surveillance during chemotherapy for improving cardiovascular outcomes), an important clinical trial, is under way to determine the impact of long-term treatment of subclinical ventricular dysfunction.[10] Some observational studies have also documented reduction of LV longitudinal strain in children and adolescents under anthracyclics, although there is no cutoff value established for the diagnosis of cardiotoxicity in this age group.[11]

The correlation between the degree of inflammatory activity and the values of strain and systolic and diastolic LV diastolic strain rate in patients with rheumatic diseases such as juvenile systemic lupus erythematosus has been demonstrated.[12] Other studies have confirmed the efficacy of strain obtained by speckle tracking in the detection of myocarditis, not only of autoimmune etiology but also of viral etiology.[13,14] The pattern of regional LV strain impairment in cases of dilated cardiomyopathy in children influences the evolution to death or to transplantation, as found by Forsha et al.[15]The authors suggest that dilated cardiomyopathy in these patients is not a single entity that presents global LV dysfunction, but a disease that compromises the strain of different ventricular segments heterogeneously, implying more or less favorable prognosis.[15] Another function of strain in cases of dilated cardiomyopathy is to detect dyssynchrony, identifying cases that may benefit from resynchronization therapy.[15]

A recent study has shown that reduction of LV longitudinal strain at the end of the first year after orthotopic heart transplantation in children can identify, with reasonable sensitivity and specificity, those individuals that will present graft vascular disease in subsequent years. The authors present the study of the myocardial strain as a noninvasive technique that could screen patients at greater risk for graft vascular disease for complementation with angiography and intravascular ultrasound, which are the methods of choice for the diagnostic confirmation of this condition.[16] Global longitudinal LV systolic peak strain values below -9% at the end of the first week of transplantation in adults are independent predictors of mortality at the end of 1 year of the procedure, for the most different causes, such as rejection, graft vascular disease and sepsis.[17] Some reports, including a small number of

transplanted children, suggest an association between the reduction of segmental strain and the presence of rejection in endomyocardial biopsies, which favors the technique as a less invasive diagnostic instrument in the near future.[18,19]

In young patients with Duchenne muscular dystrophy, studies have shown a significant reduction in longitudinal and radial strain of the LV inferolateral and anterolateral walls, even before the ejection fraction was impaired or the onset of HF symptoms. Interestingly, these areas correspond to the areas of myocardial fibrosis detected early by magnetic resonance imaging.[20] Several studies have demonstrated an improvement in the cardiovascular outcome and 10-year survival of patients with Duchenne receiving angiotensin converting enzyme inhibitors and beta-blockers at the first echocardiographic signs of myocardial deterioration, when they are still asymptomatic from a cardiovascular point of view.[21] These findings corroborate the introduction of ventricular strain analysis in the follow-up protocols for this group of patients.

The study of myocardial strain has also supported the detection of myocardial involvement in deposition diseases, such as Mucopolysaccharidoses (MPSs)[22] and Pompe disease.[23] Studies have focused on myocardial strain as a parameter to evaluate the impact of long-term enzyme replacement on the ventricular function of patients with these pathologies.[24] The use of more sensitive ventricular function parameters has become essential in a scenario where depositional diseases in childhood become chronic adult diseases due to the latest therapeutic innovations (enzyme replacement, gene therapy and bone marrow transplantation).

The analysis of myocardial strain also appears as a possibility of early diagnosis of myocardial inflammation and ventricular dysfunction in cases of Kawasaki disease. Note that the American Heart Association (AHA) proposes the use of echocardiographic evidence of ventricular dysfunction as a supporting criterion to incomplete Kawasaki diagnosis.[25] The commonly used parameter is the reduction of LV shortening or ejection fraction – known to be less sensitive than the strain analysis. McCandless et al.[26] found a reduction of LV longitudinal strain on the initial echocardiogram of patients with Kawasaki who later developed coronary dilatation or showed resistance to treatment with immunoglobulin. Patients who did not develop coronary dilatation and who promptly responded to the treatment had an LV longitudinal strain comparable to that of the healthy control group on the initial echocardiogram. These findings suggest that LV strain may soon be used as a risk stratification tool in Kawasaki.[26] However, multicenter studies, including a larger number of patients, will be required.

In cases of myocardial dysfunction induced by pediatric sepsis, LV longitudinal and circumferential strain appear to be reduced in early stages, despite the conserved ejection fraction. Studies that included a small number of pediatric patients found an association between LV strain reduction and increase of serum lactate, pointing to the potential role of strain obtained at the early echocardiogram in the categorization of the septic condition severity.[27] Prospective studies should be conducted in order to investigate the prognostic role of strain in pediatric sepsis and its impact on early therapeutic management.

In adult patients with chronic renal failure (CRF), reduced LV longitudinal strain has been confirmed, even in the early stages of the disease, with preserved ejection fraction. The early involvement of myocardial strain is attributed to chronic inflammation-induced fibrosis and uremic toxins. Besides, endothelial dysfunction accompanying CRF may lead to an inadequate vasodilator response, causing ischemia in a hypertrophic ventricle. Similar findings have also been documented in pediatric populations, and it remains to be established whether this LV longitudinal strain reduction can be used as a specific predictor of morbidity and mortality in children with CRF.[28]

Cardiovascular abnormalities are common in HIV-infected individuals, but are often underdiagnosed and untreated, which impacts quality of life and long-term mortality. They are attributed to both the direct effect of the virus and antiretroviral medications on the myocardium and vasculature. Symptomatic systolic dysfunction is usually found only in more advanced cases of AIDS. In a prospective study conducted in 2002, called the P2C2-HIV study, Starc et al. had proposed routine echocardiography scans in the follow-up of children with HIV.[29] More recent studies in children and young adults have demonstrated impairment of right ventricular (RV) and LV longitudinal strain, even in asymptomatic patients with normal LV ejection fraction. Considering these results, Naami et al.[30] have suggested the incorporation of the myocardial strain study into the echocardiograms of pediatric patients with HIV, in order to identify patients with subclinical dysfunction and higher cardiovascular risk.

A study that included adolescents and young adults with thalassemia undergoing multiple transfusions, Chen et al.[31] found a negative correlation between serum ferritin and LV longitudinal strain. Besides this, even after correction for sex, age, level of serum ferritin and ventricular mass index, LV longitudinal strain remained an independent predictor of adverse events in thalassemic patients, such as HF, arrhythmias and death (Hazard Ratio – HR: 6.05; $p = 0.033$). The authors suggest that myocardial strain analysis may help stratify cardiovascular risk in this group of patients, even though they maintain LV ejection fraction within normal limits.[31]

Investigating children and adolescents with idiopathic pulmonary hypertension (IPH), Okumura et al.[32] demonstrated the prognostic value of serial RV longitudinal strain assessment in the pediatric population. A strain value smaller than -14% at the initial echocardiogram identified patients who evolved to lung transplantation or death with 100% sensitivity and 54.5% specificity. In addition, patients who survived transplant-free did not have any significant variation in RV longitudinal strain values throughout the follow-up. They concluded that myocardial strain in pediatric IPH is a more sensitive tool than the conventional parameters for evaluating RV function (Tricuspid annular plane systolic excursion – TAPSE, FAC, and tricuspid S' wave velocity) for the detection of patients with worse prognosis.[32] In a recent paper, Hooper et al.[33] have demonstrated the usefulness of RV longitudinal strain in the clinical follow-up of pediatric IPH, demonstrating that strain values have an excellent correlation with Brain Natriuretic Peptide (BNP) values during treatment with analogues of prostacyclin.[33]

Ventricular Strain in congenital heart diseases

Analysis of RV longitudinal strain in the subpulmonary position proved feasible and reproducible in the perioperative evaluation of different congenital heart diseases.[34] However, in cases where there is significant residual obstruction in the postoperative period (PO), parameters of RV longitudinal systolic function evaluation, such as TAPSE, S' wave velocity and longitudinal systolic peak strain, do not properly correlate with the ejection fraction obtained by cardiac magnetic resonance imaging (MRI). In situations of pulmonary stenosis or a combination of stenosis and pulmonary insufficiency, RV hypertrophy leads to the predominance of circumferential fibers, altering the strain pattern of this chamber, which usually depends more on longitudinal fibers.[35] Hayabuchi et al.[36] evaluated the RV free wall circumferential systolic peak strain at the subcostal view, specifically in children with congenital cardiopathies with RV pressure overload. Thus, they found a better correlation between RV strain and ejection fraction values.[36] Studies involving asymptomatic children in late Tetralogy of Fallot (T4F) PO found a compromised biventricular longitudinal systolic peak strain. Some authors found a negative correlation between RV longitudinal systolic peak strain and RV ejection fraction and pulmonary regurgitation fraction – both estimated by CMRI.[37] Other studies have documented a negative correlation between LV longitudinal strain and degree of pulmonary regurgitation, underscoring the importance of interdependence between the ventricles.[38] Although the study of myocardial strain can detect subclinical systolic dysfunction in patients operated for T4F, presenting pulmonary regurgitation, unfortunately, there is no consensus regarding a cut-off strain value that points out the best moment for pulmonary valve replacement.

RV in a systemic position also demonstrates a change in the myocardial strain pattern, with predominance of contraction of circumferential fibers. Discrete reduction of longitudinal strain in this condition represents an abnormal right ventricular geometry and actual non-systolic dysfunction. This is an adaptive mechanism that makes systemic RV contractility similar to that of LV. For this reason, recent studies suggest a range of normal systemic RV longitudinal systolic strain values, which are lower than expected for subpulmonary RV (-10% to -14.5%).[35] RV longitudinal strain values smaller than -10% were associated with adverse events in late Senning surgery PO.[39]

The selection of patients with Single Ventricle (SV) for Fontan surgery considers pulmonary vascular resistance and ventricular end-diastolic pressure. However, the current indication criteria are flawed for a considerable portion of these patients, who endure complications and prolonged hospitalizations. Park et al.[40] demonstrated that the preoperative circumferential strain rate is independently associated with a length of stay longer than 14 days. When associated with pulmonary vascular resistance and ventricular end-diastolic pressure, preoperative circumferential strain rate improves risk stratification for patients with SV, candidates for the Fontan surgery, regardless of whether the ventricle is of right or left morphology.[40]

In the case of Ebstein's anomaly, the study of myocardial strain adds little to the evaluation of right ventricular function, since the strain has a poor correlation with the ejection fraction obtained by CMRI.[41]

Castaldi et al.[42] demonstrated the usefulness of LV longitudinal strain in the diagnosis of patients with coronary artery obstruction in late PO of surgical correction of anomalous origin of the left coronary artery from the pulmonary artery. Strain value <-14.8% at the echocardiogram identified myocardial segments with fibrosis at CMRI with 92.5% sensitivity and 93.7% specificity. Interestingly, all patients had preserved LV systolic and diastolic function at the conventional echocardiogram.[42]

Dusenbery et al.[43] reinforced this association between LV longitudinal strain reduction and the presence of myocardial fibrosis, evaluating children and young adults with aortic valve stenosis and preserved LV ejection fraction. The authors found late enhancement after administration of gadolinium in CMRI in the same myocardial segments that presented reduced longitudinal systolic peak strain values at the echocardiogram. It is known that adults with aortic stenosis presenting late enhancement on gadolinium-based CMRI and reduced LV longitudinal strain values have higher mortality rates after valve intervention. Further prospective studies should be performed in children to establish the prognostic value of LV longitudinal strain reduction in pediatric populations with aortic valve stenosis.[43]

Right and left atrial strains in pediatrics

The study of right atrial mechanics using speckle tracking has been recently incorporated into pediatrics, emerging as a promising tool for the detection of right ventricular dysfunction. Hope et al.[44] found a significant reduction of right atrial longitudinal strain in children with IHP. Atrial strain was proven more sensitive and specific than conventional parameters for the evaluation of right ventricular function in the identification of patients with IHP who presented unfavorable outcomes (death, lung and/or heart transplantation). [44]

Several studies have described the clinical implications of left atrial strain measurement by the speckle tracking technique. LA strain in the reservoir phase was more accurate in the estimation of LV end-diastolic pressure than classical echocardiographic parameters such as left atrial volume and E/E' ratio, in addition to inversely correlating with plasma levels of the N-terminal (NT)-pro hormone B-type natriuretic peptide (BNT-ProBNP). Many congenital heart defects are associated with reduced ventricular compliance, which leads to increased pressure and atrial remodeling. Studies that include the analysis of the atrial strain may contribute to a better understanding of diastolic dysfunction in these conditions.[45]

Perspectives of using ventricular strain on fetal echocardiography

Recent studies suggest that myocardial strain analysis may contribute to the evaluation of biventricular systolic and diastolic function in fetuses. As an example, Miranda et al.[46] documented a reduction of early and late diastolic strain rate in the RV and LV longitudinal axis in fetuses from diabetic mothers. The authors emphasize that the impairment of diastolic strain was unrelated to the presence of septal hypertrophy. In addition, they recorded a reduced RV longitudinal systolic peak strain, in comparison with normal

fetuses of the same gestational age. They concluded that the study of myocardial strain can detect subclinical disorders in the ventricular function of fetuses of diabetic mothers, before the classic echocardiographic parameters are able to do so.

Further prospective studies should be conducted in order to prove the usefulness of strain analysis in the evaluation of fetal ventricular function, incorporating it into the routine of care.[46]

Closing remarks

The study of myocardial strain using the two-dimensional speckle tracking technique has been gaining more space in pediatric echocardiography, appearing as a promising alternative for the diagnosis of subclinical dysfunction in this population. As soon as normal strain values can be used as a universal reference in pediatrics, this tool must be naturally incorporated into the routine of care.

Authors' contributions

Research creation and design: Leal GN; Data acquisition; Analysis and interpretation of data: Leal GN; Statistical analysis: Leal GN; Manuscript writing: Leal GN; Critical revision of the manuscript as for important intellectual content: Leal GN.

Potential Conflicts of Interest

There are no relevant conflicts of interest.

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