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Regional Left Ventricular Myocardial Mechanics in Degenerative Myxomatous Mitral Valve Disease

A Comparison Between Fibroelastic Deficiency and Barlow's Disease

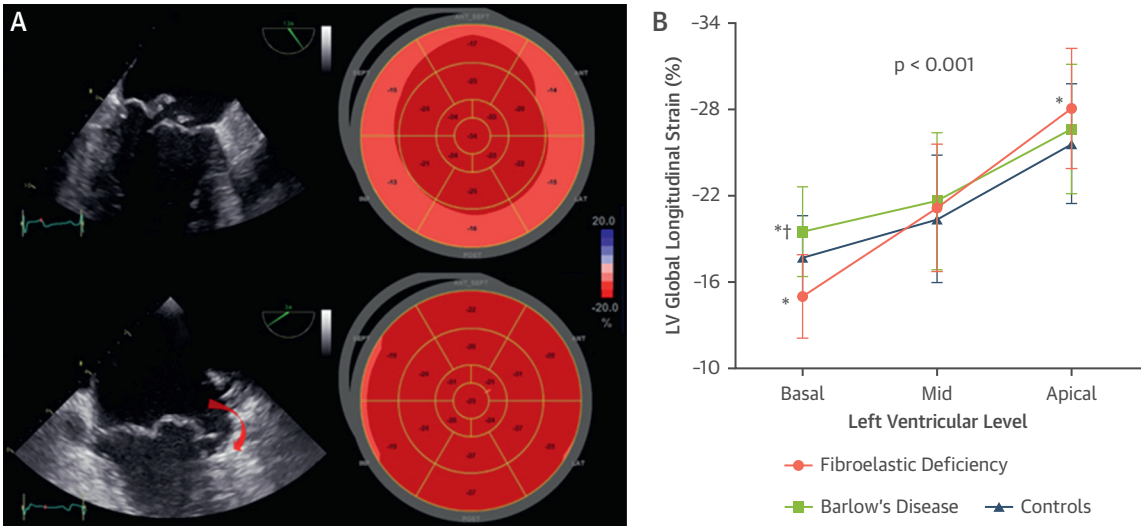
Fibroelastic deficiency (FED) and Barlow disease (BD) are 2 phenotypes of degenerative mitral valve regurgitation characterized by excessive movement of the mitral leaflets and the saddle-shaped mitral annulus (1,2). Compared with FED, BD exhibits more pronounced excessive mitral annulus motion and characteristic late systolic flattening (2). This finding may be related to enhanced function of the basal segments of the left ventricle and weaker mitral valve annulus leading to more pronounced late systolic mitral regurgitation (MR) in BD. It has been suggested that fixation of the hyper-enhanced annular dynamics with a ring annuloplasty may be sufficient to restore mitral valve competence.

The hypothesis of the present study was to show whether BD has different left ventricular (LV) mechanics compared with FED that may explain the different mechanism of MR. In 104 patients with FED (n = 62) or BD (n = 42) with moderate to severe MR and 40 healthy subjects, transthoracic echocardiography and 2-dimensional speckle tracking strain analyses were performed to assess LV global longitudinal strain and level-based longitudinal strain (basal, mid, and apical) (EchoPAC BT13, GE Medical Systems, Horten, Norway) (**Figure 1A**). Comparisons between patients with FED, patients with BD, and control subjects were performed using linear mixed models.

Patients with FED were more symptomatic, more frequently had atrial fibrillation, and had a higher use of diuretic agents compared with patients with BD. No other differences in clinical characteristics were noted. LV volumes and left atrial diameter were larger in patients with FED and BD compared with control subjects, but only those with FED exhibited lower ejection fraction (58 ± 8%, 62 ± 7%, and 63 ± 5%, respectively; p = 0.001). Mitral regurgitant volumes were also similar between the FED and BD groups (52 ± 17 ml and 46 ± 18 ml; p = 0.160). LV global longitudinal strain did not differ across the groups after correcting for age, sex, and LV end-systolic and end-diastolic volumes (control subjects: −21.5 ± 1%; patients with FED: −19.8 ± 3%; patients with BD: −21.4 ± 3%; p = 0.091). A gradient in LV strain per level was noted in all groups, with lower values in the basal levels and higher values in the apical levels (**Figure 1B**). This gradient differed across the groups: patients with FED exhibited impaired LV strain at the basal levels but enhanced values at the apical levels compared with control subjects, whereas patients with BD had enhanced LV strain in the basal levels compared with both control subjects and patients with FED. This finding suggests that in patients with FED, valvular incompetence may be exclusively a valvular problem, whereas in patients with BD, the hyper-enhanced function of the LV basal segments may contribute to a functional prolapse.

Changes in regional LV forces may have a crucial role in abnormal annulus dynamics as hyper-enhanced LV strain in the basal segments could explain why the annulus is hyperdynamic at late systole: the mitral annulus, which is exposed to

FIGURE 1 Regional Assessment of LV Longitudinal Strain in Barlow Disease and Fibroelastic Deficiency



(A) Examples of mitral regurgitation due to fibroelastic deficiency **(top)** and Barlow's disease **(bottom)** and the corresponding left ventricular (LV) longitudinal strain bull's-eye plots. In the fibroelastic deficiency mitral regurgitation, LV basal levels exhibit more impaired LV strain values than in Barlow disease mitral regurgitation. **(B)** Longitudinal strain values per LV level (basal, mid, and apical) for control subjects **(blue)** and patients with fibroelastic deficiency **(pink)** and Barlow's disease **(green)**. *Significant p value versus the same level in controls; †significant p value in Barlow's disease versus fibroelastic deficiency.

increased LV dynamics, is pulled outward at late systole, leading to annular dilatation, flattening, and leaflet malcoaptation (Figure 1A). Huttin et al. (3) reported the presence of abnormal strain in the LV segments characterized by increased post-systolic shortening in patients with mitral valve prolapse; however, no distinction was made between FED and BD. The present study is thus the first to characterize regional LV strain in these 2 etiologies of degenerative MR.

One of the limitations of the present study is the lack of sequential data to investigate how LV mechanics change across various grades of MR and at different time points. The chronicity of MR may affect LV mechanics differently according to the phenotype of degenerative MR. Better understanding of LV mechanics and its relation to mitral annulus dynamics in FED and BD can aid the decision-making in surgical techniques. Implantation of an annulus ring will help stabilize the hyper-enhanced LV basal segments in BD. Due to the small sample size, this study should be considered as hypothesis generating, and further validation with larger populations is necessary.

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Thrombus-Related Coronary High-Intensity Signal on T1-Weighted Magnetic Resonance Imaging Is a Potential Predictor of Adverse Cardiovascular Events After Stent Implantation

The presence of underlying vulnerable plaques, especially thrombus, has the potential to influence arterial healing and possibly long-term outcomes in patients with angina pectoris after percutaneous coronary intervention (PCI) (1). T1-weighted imaging (T1WI) with noncontrast magnetic resonance (MR) can effectively assess coronary intraluminal thrombus through a high-intensity signal (HIS), determined by the plaque-to-myocardial signal intensity ratio (PMR) (2). We identified the optimal PMR cutoff value for predicting optical coherence tomography (OCT)-defined intraluminal thrombus and investigated the prognostic value of the target lesion HIS among patients with angina who underwent OCT-guided stent implantation.

A total of 103 patients with either stable (n = 42) or unstable (n = 61) angina, who underwent MR within 24 h before the day on which OCT-guided PCI was performed, were prospectively examined. All patients were scanned using a 1.5-T MR imager (Achieva, Philips Medical Systems, Best, the Netherlands) with a 5- or 32-element cardiac coil. Coronary target plaque images were obtained using a 3-dimensional T1WI, inversion recovery, and fat-suppressed black-blood gradient-echo sequence with navigator-gated free-breathing and electrocardiogram-gated techniques (2). After the optimal PMR cutoff value for the prediction of OCT-defined thrombus was identified, target lesions with a PMR higher than the cutoff value were classified as HIS. In addition, HIS were further divided into intrawall and intraluminal HIS based on localization by using cross-sectional T1WI (**Figure 1A**) (2). Major adverse cardiac and cerebrovascular events (MACCEs) were defined as the composite of cardiovascular death, nonfatal acute coronary syndrome, stroke, unplanned de novo PCI, and target lesion revascularization.

During the follow-up period (median 1,123 days), MACCEs were observed in 23 patients. PMR values ($p = 0.036$) and the frequency of OCT-defined thrombus ($p = 0.0073$) were significantly higher in patients who developed MACCEs than in those who did not. No significant differences in stent type and minimum stent area after PCI were found. Receiver-operating characteristic curve analysis showed that the optimal PMR cutoff value for OCT-derived thrombus was 1.20 (area under the curve: 0.77; $p = 0.0024$). According to the PMR and localization of HIS, patients were divided into 3 groups: non-HIS (n = 54), intrawall HIS (n = 24), and intraluminal HIS (n = 25) (**Figure 1A**). Intraluminal HIS were strongly associated with OCT-derived thrombus (non-HIS: 11%, intrawall HIS: 17%, intraluminal HIS: 76%; $p < 0.001$), and had the highest incidence of overall MACCEs among the 3 groups (11% vs. 29% vs. 40%; $p = 0.011$). The cardiovascular death rates were 0%, 4%, and 4%; the stroke rates were 0%, 4%, and 4%; the unplanned de novo PCI rates were 7%, 13%, and 4%; and target lesion revascularization rates were 4%, 8%, and 16% in the non-HIS, intrawall HIS, and intraluminal HIS groups, respectively. All 3 acute coronary syndrome events occurred in the intraluminal HIS group. The Kaplan-Meier curve for MACCEs revealed that a trend toward having MACCEs was observed in patients with intrawall HIS compared with non-HIS ($p = 0.052$). Further, intraluminal HIS showed a significantly higher rate of MACCEs than that shown by non-HIS ($p < 0.01$) (**Figure 1B**). Multivariate Cox regression analysis identified 3-vessel disease (hazard ratio: 4.22; 95% confidence interval: 1.39 to 12.90; $p = 0.012$), and the presence of intraluminal HIS at the target lesion (hazard ratio: 2.88; 95% confidence interval: 1.01 to 9.11; $p = 0.049$) as significant predictors of MACCEs.

Although PCI with drug-eluting stents markedly improved clinical outcomes, serious concerns about late complications remain, such as in-stent neoatherosclerosis, which is an important substrate for in-stent restenosis and late stent thrombosis (1). Intraluminal HIS may indicate that a large number of thrombi develop from plaque rupture based on the presence of vulnerable complex plaques associated with a necrotic core and intraplaque hemorrhage. The presence of large thrombus-related vulnerable lesions with intraluminal HIS may be reflected in the higher occurrence of late stent failure and may cause differences in the rate of target lesion-related events between intrawall and intraluminal HIS. In the present study, MACCEs also