

significantly higher proportion of IHIS in ICA plaques ipsilateral to the side of infarction in cryptogenic stroke patients ( $p < 0.001$ ), but not in patients with strokes from cardioembolism ( $p = 0.76$ ) or small-vessel occlusion ( $p = 0.49$ ).

Our results suggest that some strokes from large-artery atherosclerosis are currently not being recognized as such because the plaque causes  $<50\%$  stenosis. Our findings also suggest that useful plaque composition data can be extracted using only a standard luminal imaging technique (time-of-flight MRA) that can be integrated into a rapid acute stroke imaging protocol. Because our IHIS-positive subgroup was small ( $n = 31$ ), larger confirmatory prospective studies are now warranted which should also investigate stroke recurrence rates in such patients. Such studies are important because if patients who are currently labeled as cryptogenic stroke are more correctly identified as harboring a culprit large-artery atherosclerotic lesion, they may benefit from intensified and targeted therapy aimed at reducing their risk of recurrent stroke and other major adverse cardiovascular events.

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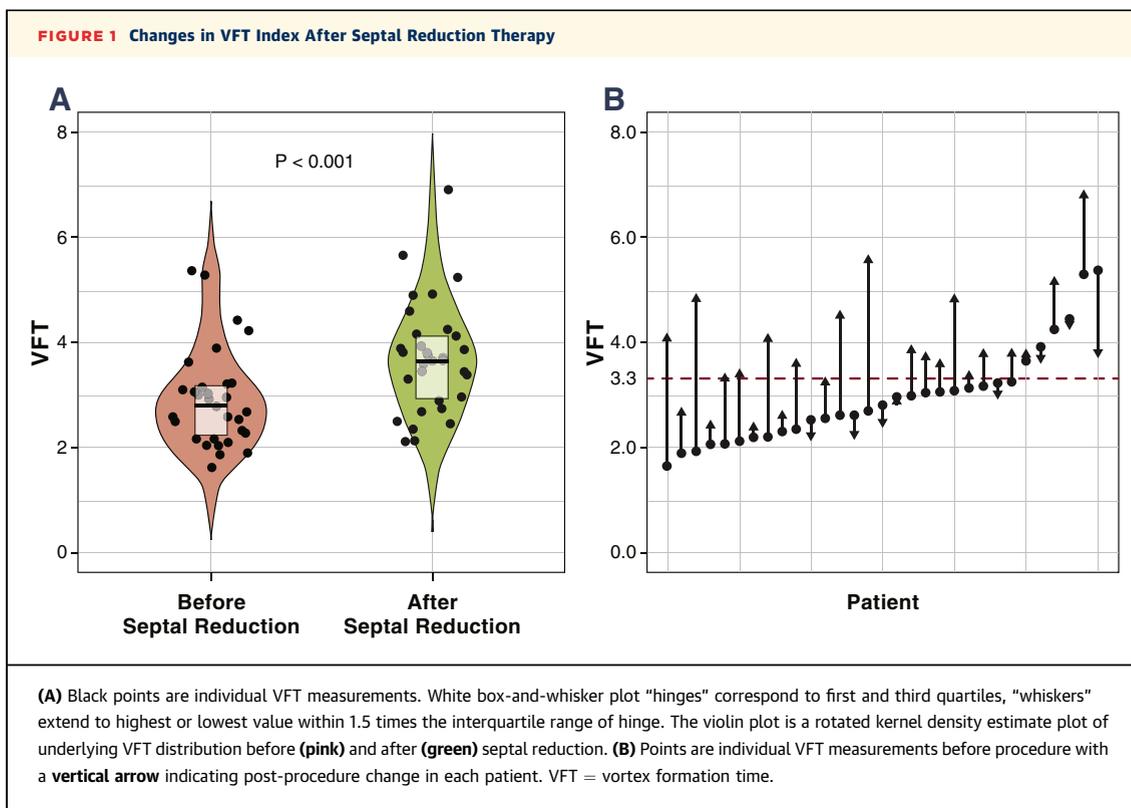
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## Vortex Formation Time Index in Patients With Hypertrophic Cardiomyopathy



Vortex ring formation in early diastole helps with left ventricular (LV) filling without an increase in left atrial (LA) pressure. Vortex formation time (VFT) is a dimensionless parameter derived from LV geometry and indexes of LV systolic and diastolic performance (1). The optimal range was reported at  $3.3 < VFT < 5.5$  but varies on the basis of cardiac pathology. VFT application in hypertrophic cardiomyopathy (HCM) has not been evaluated. We sought to study VFT in relation to exercise tolerance in HCM.

We included 116 HCM patients (mean age 58 years; 39.7% female). Patients willing and able to exercise ( $n = 77$ ) underwent exercise testing using a modified Bruce protocol within 2 months or less of a transthoracic echocardiography (TTE) study. Cardiac magnetic resonance findings were noted for 94 patients who underwent imaging within 4 days of TTE. Patients with previous septal reduction, more than mild valve disease, prosthetic valves, moderate or worse annular calcification, and atrial fibrillation were excluded. Normal healthy subjects ( $n = 20$ ,  $48 \pm 7.4$  years of age) were included. To examine the impact of septal reduction on VFT, patients who underwent alcohol septal ablation ( $n = 24$ ) or surgical myectomy ( $n = 7$ ) were examined. Analysis was performed, blinded to clinical data, for LV and LA volumes and left ventricular ejection fraction (LVEF), mitral annulus diastolic diameter (D) and velocities (mitral peak early diastolic velocity [E], mitral peak late diastolic velocity [A], ratio of mitral peak early diastolic velocity to mitral peak late diastolic velocity [E/A], atrial filling fraction [AFF]), mitral annulus early diastolic velocity ( $e'$ ), (pulse Doppler: septal, lateral, average), and ratio of mitral peak early diastolic velocity to mitral annulus early diastolic velocity ( $E/e'$ ). left ventricular outflow tract (LVOT) gradient was measured at rest and with the Valsalva maneuver. LV diastolic function was graded per guidelines (2). The VFT was obtained:  $4 \times (1 - \beta) \times \alpha^3 \times LVEF/\pi$  (1), ( $\alpha = LVEDV [LV \text{ end-diastolic volume}]^{1/3}/D$ ,  $\beta$  is the fraction of stroke volume due to AFF). The study population was divided into VFT  $< 3.3$  and  $3.3$  to  $5.5$ . The Wilcoxon rank sum and Student  $t$  tests were used to determine the differences in continuous variables. Differences before and after treatment were tested



with paired Student *t*/Wilcoxon signed rank tests for continuous data.

New York Heart Association (NYHA) functional class was lower in patients with a VFT  $\geq 3.3$  than in those with a VFT  $< 3.3$  ( $p = 0.048$ ). Most had asymmetrical hypertrophy (93.1%), with no significant differences in hypertrophy pattern, maximal/septal thickness, LV mass (cardiac magnetic resonance), or scar burden between the 2 groups. Patients with a VFT  $< 3.3$  had a smaller LVEDV ( $p = 0.002$ ) and stroke volume, larger AFF ( $p \leq 0.001$  for both), and borderline EF difference ( $p = 0.056$ ). Rest and provoked LVOT gradients  $> 30$  mm Hg were more frequent in patients with a VFT  $< 3.3$  ( $p = 0.024$ ).

The VFT index was not significantly different in controls versus HCM (control subjects:  $3.6 \pm 0.4$ ; HCM patients:  $3.1 [2.4 \text{ to } 4.1]$ ;  $p = 0.07$ ). Significant differences were present between 2 HCM groups separated by VFT in LA volume index,  $e'$  velocity, and diastolic dysfunction grade such that patients with a VFT  $< 3.3$  had more advanced diastolic dysfunction ( $p < 0.01$ ). Patients with a VFT of 3.3 to 5.5 achieved higher workload and maximal oxygen consumption than patients with a VFT  $< 3.3$  (both  $p < 0.01$ ).

After septal reduction, the VFT index significantly increased (Figure 1) and NYHA functional class

decreased ( $p < 0.001$ ). LVEDV and stroke volume increased ( $p < 0.05$ ), and septal thickness decreased ( $p < 0.001$ ) as did LA volume index and mitral annulus diameter ( $p < 0.04$  for the decrease in both variables). LVOT gradient, E/A, and E/ $e'$  decreased significantly ( $p < 0.03$ ). For the 16 patients with exercise testing, a significant correlation was present between change in the VFT and that in maximal oxygen consumption ( $r = 0.9$ ,  $p < 0.001$ ).

Exercise tolerance is affected in part by LV stroke volume and filling pressures. Higher exercise peak oxygen consumption occurs with preserved LV stroke volume. HCM patients with a VFT index between 3.3 and 5.5 had a higher LV stroke volume associated with lower LV filling pressures. This is likely due to the important contribution of efficient energy transfer to LV filling via a better developed vortex ring.

In conclusion, VFT is a single index that can be derived from standard 2-dimensional and Doppler parameters. The study shows its clinical relevance to LV diastolic function in HCM and more importantly to exercise tolerance before and after septal reduction. This is of interest as exercise tolerance is one of the major predictors of outcome in HCM.

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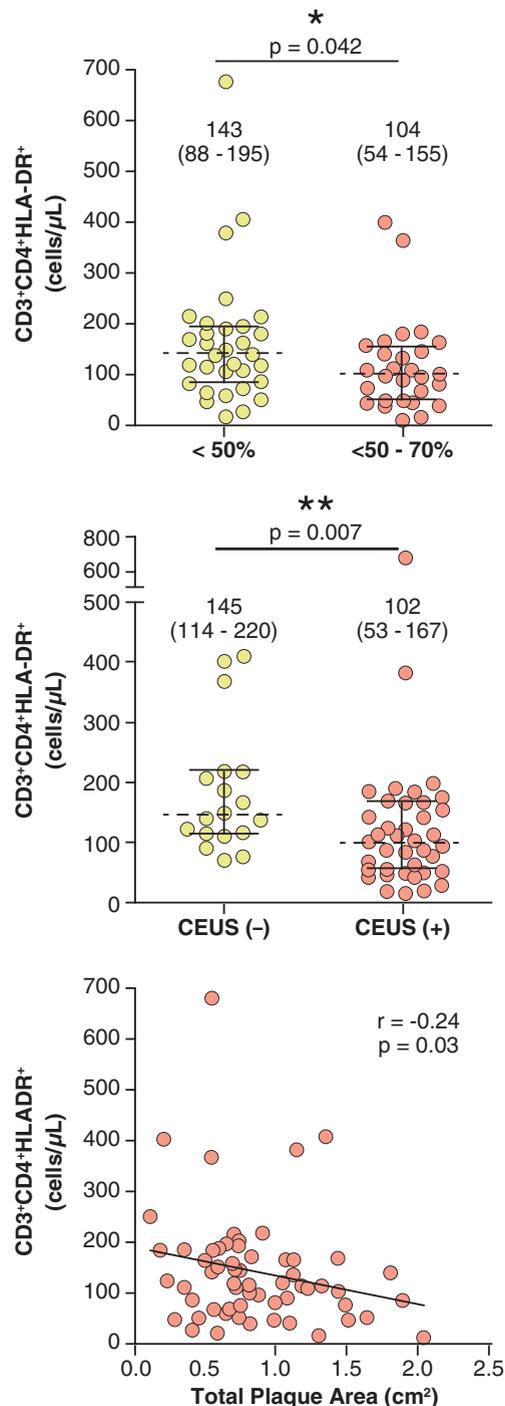
**Reduction of Circulating HLA-DR<sup>+</sup> T Cell Levels Correlates With Increased Carotid Intraplaque Neovascularization and Atherosclerotic Burden**



Alteration of circulating T-cell subpopulations may reflect the local immune process in plaques (1), providing insights on atherosclerosis pathogenesis. Only limited knowledge concerning the relationship between circulating lymphocytes and features of atherosclerotic lesions is available (2). We evaluated the relation between ultrasonographic and contrast-enhanced ultrasound (CEUS) characteristics of carotid artery plaques and selected circulating CD4<sup>+</sup> T-cell subpopulations in patients with an asymptomatic carotid artery stenosis of intermediate severity without indication for carotid endarterectomy or stenting.

Between April 2012 and July 2014, we enrolled 60 consecutive patients (53% men; mean age 69 ± 8 years). Seventy-three percent had dyslipidemia (64% receiving statins), 77% systemic hypertension, 23% diabetes mellitus, and 22% with a history of coronary heart disease. Patients provided written

**FIGURE 1** Circulating Number of CD4<sup>+</sup>HLA-DR<sup>+</sup> T Cells Is Decreased in Patients With Increased Carotid Intraplaque Neovascularization and Atherosclerotic Burden



Levels of HLA-DR<sup>+</sup> T cells in relation to degree of carotid plaque stenosis (top) and the presence of contrast-enhanced ultrasound+ plaques in each patient (middle). Total plaque area in relation to HLA-DR<sup>+</sup> T cells (bottom). Mann-Whitney U test and Spearman rank correlation coefficient were used.