The E-Wave Propagation Index (EPI): A Novel Echocardiographic Parameter for Prediction of Left Ventricular Thrombus.

Derivation from Computational Fluid Dynamic Modeling and Validation on Human Subjects.

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Abbreviations:

CAD: Coronary artery disease
CFD: Computational fluid dynamic
CMP: Cardiomyopathy
CT: Computed Tomography
EDV: End diastolic volume
EF: Ejection fraction
EPI: E-Wave Propagation Index
ESV: End systolic volume
HFrEF: Heart failure with reduced ejection fraction
ICMP: Ischemic cardiomyopathy
LVEDV: left ventricle end diastolic volume
LVEF: left ventricular ejection fraction
LVL: Left ventricle length
LVT: left ventricle thrombus
NICMP: Non-ischemic cardiomyopathy
SV: Stroke volume
VTI: Velocity time integral

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Abstract:

Background: To describe the derivation and validation of a novel echocardiographic metric for prediction of left ventricle thrombus (LVT).

Methods: Computational fluid dynamic modeling using cardiac CT images was used to derive a novel echocardiography-based metric to predict the presence of LVT. We retrospectively, reviewed 25 transthoracic echocardiograms showing definite LVT (LVT group). We then randomly selected 25 patients with LVEF >=55% (Normal EF group) and 25 patients with severe cardiomyopathy (CMP) with LVEF <=40% without evidence of LVT (CMP group). The E-wave Propagation Index (EPI) was measured as the E-wave velocity time-integral divided by the LV length. An EPI>1 indicates penetration of the mitral jet into the apex whereas an EPI<1 is indicative of incomplete apical washout. The mean EPI was compared between the three groups. Crude and adjusted odd ratios of EPI and LVT association were also measured.

Results:
Mean EPI was highest for the normal EF group and lowest in the LVT group (1.7 vs. 0.8; p<0.0001). Mean EPI also differed significantly between LVT and CMP groups (0.8 vs. 1.2; p<0.0001). 88% of the LVT group had EPI <1.0 compared to only 20% of the CMP group (p<0.0001). Among the LVT and CMP groups, an EPI <1 increased the odd ratio of LVT by 53.7 times (95% CI: 6.9-416) controlling for LVEF and LV volume.

Conclusions
The E-wave propagation index is a novel, easily-obtainable, echocardiographic metric to evaluate apical LV flow. An EPI of less than 1 is an independent predictor of LVT formation.

Introduction:

Left ventricular thrombus (LVT) is an important clinical sequela of acute myocardial infarction and chronic severe cardiomyopathy. The risk of LVT development has decreased in the past

decade because of the adaption of early revascularization therapy for the treatment of acute myocardial infarction (MI) and ranges from 10% (1) to 23% (2,3). Less is known about the prevalence of LVT in chronic cardiomyopathy or heart failure with reduced left ventricular ejection fraction (HFrEF). Left ventricular thrombus was detected in 6% of patients with chronic cardiomyopathy (4). Despite decreasing prevalence, LVT remains an important complication of acute anterior MI and severe chronic cardiomyopathy causing significant morbidity related to stroke or/and systemic embolization. The presence of LVT increases risk of systemic embolism by 5.4 times (5) but currently used methods to predict LVT development in both acute and chronic cardiomyopathy conditions, lack specificity and sensitivity.

Left ventricular thrombus is caused by myocardial cell injury along with regional blood stasis, mostly at the LV apex, causing activation of the coagulation cascade. Studies show that abnormal LV apical flow is the most important factor in predicting LVT development (6-8). However, the previously described methods to characterize abnormal LV blood flow lack sensitivity and specificity and are difficult to measure for every day clinical use.

Computational fluid dynamics (CFD), which refers to the solution of fluid flow equations on a computer, has recently emerged as a new modality for the analysis of hemodynamics (9,10). Significant advances in computational power of modern day computers and improvement of spatial resolution of cardiac imaging techniques like cardiac computed tomography (CT) have made it possible to apply CFD modeling to study blood flow in humans (11).

In this study, based on CFD analysis of canonical and patient-specific models of the LV, we propose a novel echocardiography-based metric that has the potential to help stratify patients with acute and chronic cardiomyopathy according to their risk of LVT development, and potentially help guide anticoagulation therapy. We call this metric the E-Wave Propagation Index (EPI). We retrospectively evaluate the ability of this metric to stratify LVT risk in a cohort of patients with and without LVT.

Methods:

CFD modeling and Derivation of EPI:

The derivation of EPI as an index for LVT risk is based on computational fluid dynamic (CFD) modeling studies. These CFD models assume blood to be an incompressible, Newtonian flow (9). For the generation of subject-specific models, 4D cardiac CT images were employed to generate time-evolving geometry of the LV lumen that closely match the kinematics of the LV lumen, including key parameters such as heart rate, end-diastolic and end-systolic volumes(EDV & ESV), ejection-fraction (EF), stroke volume (SV) and E/A ratio (12).

Our computational model includes coupling of the LV blood flow with a biochemical model of extrinsically activated coagulation cascade wherein, tissue-factor exposed at the infarcted LV walls leads to the generation of thrombin through a multistep reaction. Subsequently, this thrombin activates platelets, polymerizes fibrinogen into fibrin and leads to the deposition of activated platelets on the lumen wall. All of the above processes are included in the current modeling approach (9).

A number of canonical (reported in (13)) as well as patient-specific cases were simulated (see supplementary video 1). Figure 1 shows results of CFD simulation for a patient with history of left anterior descending (LAD) occlusion and persistent anteroapical wall akinesis. Simulations indicate that the accumulation of thrombin in the apical region, which is a key indicator of thrombogenic risk, depends directly on the ability of the diastolic mitral jet, to reach and "wash out" the apex. For the case in Fig. 1, the mitral jet from the E-Wave does not propagate to the apex at the end of diastole. Other cases, (supplementary video 2 and 3) indicated varying degrees of mitral jet propagation as well as thrombin accumulation.

The CFD results show (Fig. 1) that the mitral jet propagates towards the apex mainly during the E-wave. A mitral jet that propagates further towards the apex during the will produce significant apical washout. Thus, the propagation distance of the mitral jet into the LV by the end of the E-wave (denoted here by L_{MJ}) indexed by the length of the LV (L_{LV}) should correlate well with apical "washout," and therefore, with LVT risk. This unit-free index, which we call the E-Wave Propagation Index (EPI) (Figure 2) is therefore given by:

$$EPI = \frac{L_{MJ}}{L_{LV}} \tag{1}$$

An EPI >=1.0 would indicate that the early diastolic (E-wave) mitral jet propagates all the way to the LV apex and washes out the apical endocardium, while an EPI <1.0 indicates poor or incomplete apical washout. The EPI combines information about LV function (stroke volume, heart rate, E/A ratio) as well as anatomy (LV length, average mitral valve area) into a single, distinct parameter.

The LV length (L_{LV}) can be measured in a straightforward manner from any transthoracic echocardiography (TTE). Echocardiography also readily provides the E-wave velocity-time-integral (VTI_E), which is given by

$$\mathrm{VTI_E\,(cm)} = \int_0^{T_E} V_M(t)\,dt \tag{2}$$

where $V_M(t)$ (cm/s) is the echo Doppler-based estimate of the flow velocity in a sample volume at the tip of the mitral leaflets and T_E is the duration of the E-wave. Under the assumption that the velocity of the jet as it propagates down towards the apex, does not vary significantly from the value estimated near the mitral leaflets, VTI_E is a reasonable estimate of L_{MJ}. Thus, EPI can be estimated via echocardiography as follows: (figure 2)

$$\mathrm{EPI} = \frac{\mathrm{VTI_E}}{\mathrm{L_{LV}}} \tag{3}$$

Patient selection: We conducted a retrospective analysis of 75 patients who had transthoracic echocardiograms (echo) done at our institution. From our echo lab data base, we selected 25 patients whose echocardiograms showed definite evidence of LVT. This group is called the LVT group (LVT group). We then randomly selected 25 patients whose echocardiograms showed a reduced LVEF of < 40%, and no LVT. These patients were not on anticoagulation therapy and had no prior stroke, TIA or systemic embolism. This group is referred to as the cardiomyopathy group (CMP group). Additionally, we randomly selected 25 patients whose echocardiograms showed normal LVEF of >=55%, normal regional wall motion and no LVT. This group is called the normal EF group (normal EF group). Selection for the CMP group and the normal EF group was performed by examining consecutive echocardiograms in our echo lab for different clinical

indications. All echocardiographic images were reviewed by the study team. Patients that fulfilled the inclusion criteria were selected. The review process continued until 25 patients within the normal EF group and another 25 patients within the CMP group were selected.

All echocardiograms were performed for routine clinical care of patients in our institutions. Echocardiograms were reviewed independently by the study team and the following parameters were extracted: stroke volume, E-wave peak velocity, E-wave VTI , left ventricular end diastolic length (LVL) and LVEF. Mitral inflow spectral Doppler was done as part of the routine transthoracic echo protocol at our institution for diastolic function evaluation by placing the sample volume at the tip of the mitral valve leaflets. Left ventricular length was measured from the 4-chamber view as the distance from the mitral annulus level to the endocardial border of the left ventricular apex (14).

Left ventricular EF was measured semi-quantitatively in our echo lab using visual assessment by a cardiologist experienced in reading echocardiograms and the Simpson's method. For purposes of our study, we used the LVEF reported in the final official echo report. When the LVEF was given as a range, the mean of that range was used. Left ventricular end diastolic volume (LVEDV) was measured from either single plane or biplane apical 4-chamber and apical 2-chamber views using summation of discs method. We defined LVT as an echogenic mass with well-defined margins adjacent to an akinetic myocardial segment of the LV visible throughout the cardiac cycle.

The E-wave Propagation Index (EPI) was measured as a unit-free parameter obtained by dividing the E-wave VTI by the end diastolic LV length. An EPI >=1.0 indicates that the early

diastolic (E-wave) blood flow wave has the ability to propagate through the length of the LV and wash the apical endocardium, while a low (EPI <1.0) indicates poor apical washout. Therefore, patients who had EPI <1.0 were categorized as having poor apical flow while those with EPI >=1.0 are categorized to have good apical flow. The higher the EPI, the more vigorous the apical blood flow.

In order to evaluate the effect of EPI on development of LVT in a prospective way, we examined the medical records of the LVT group to review any echocardiograms that were done prior to the index echo (the echo that showed the LVT). From those prior echocardiograms, the LVEF was obtained and the absence of LVT was verified. Additionally, the EPI was measured from these prior echocardiograms and compared to the EPI obtained from the index echo. The time interval between the index echo and the prior echo was also recorded.

Any patient with echocardiograms of poor image quality that limited assessment of the presence or absence of LVT was excluded. Echocardiograms that showed poor-quality mitral inflow Doppler signals or atrial fibrillation were also excluded. Relevant clinical and demographic variables were obtained for the study population such as age, gender, and comorbidities. For the LVT group, the etiology of the cardiomyopathy was categorized as ischemic or non-ischemic based on chart review. Patients within the LVT group were also categorized into chronic cardiomyopathy or acute cardiomyopathy. Patients who developed LVT within 4 months post-acute MI or in the setting of acute initial heart failure presentation and had no known history of cardiomyopathy in the past 4 months are considered to have acute presentation of acute cardiomyopathy. The rest of the LVT group is categorized as having chronic presentation or chronic cardiomyopathy.

Descriptive data including means, and standard deviations were used to describe continuous variables. Percentages were used to describe categorical variables. When two means were compared, the Mann-Whitney test was used, while the Kruskal-Wallis test was used to test the difference among more than two means. The Fisher exact test was used to test for differences in categorical variables. A $P < 0.05$ was designated as significant. Logistic regression analysis was used to calculate the crude odd ratio (OR) of the presence of LVT in those with EPI <1 compared to those with EPI >=1 in the CMP group. Adjusted OR by LVEF and LV volume was also calculated.

The study was approved by the institutional review board of the institution. All analyses and data management were done using SAS 9.3 for Windows (SAS Institute, Inc., Cary, NC) statistical software package.

Results:

The clinical and echocardiographic characteristics of the study population are summarized in Table 1. The mean age for LVT group was 55.1 years compared to 61.3 and 56.7 years for the CMP and normal EF groups, respectively (p=0.05). The majority (76%) of the LVT and CMP groups were men compared to only 48% of the normal EF group (p=0.07). Active tobacco smoking was more prevalent within the LVT group (24%) compared to the CMP group (4%) or the normal EF group (8%) (p=0.13). Coronary artery disease was the cause of cardiomyopathy in 14 patients (56%) of the LVT group and 9 patients (36%) of the CMP group (Table 1).

When the LVT group was compared to the CMP group, both groups had markedly reduced LVEF. Mean LVEF for the LVT group was 20.2% versus 24.7% for the CMP group (p=0.02). Although the LVT group had slightly lower LVEF, there was no significant difference in LVEDV or LV end-diastolic length. (Table 1 &2)

The EPI differed significantly between the three groups. Mean EPI was highest for the normal EF group and lowest in the LVT group (1.7 vs. 0.8; p<0.0001). Mean EPI also differed significantly between LVT and CMP groups (0.8 vs. 1.2; p<0.0001). (Figure 3)

Furthermore, when EPI was categorized as a binary variable, low EPI (EPI<1) was much more prevalent in the LVT group than in those with CMP without LVT: 88% of the LVT group had EPI <1.0 compared to only 20% of the CMP group (p<0.0001). None of the patients within the normal EF group had EPI <1.0 (Figure 4). Among the LVT and CMP groups, the crude odd ratio (OR) of the presence of LVT among those with EPI <1 compared to those with EPI >=1 is 29.3 (95% CI: 6.2-138.7, p <0.0001). This OR remains clinically and statistically significant even after controlling for LVEF and LVEDV with an adjusted OR of 53.7 (95% CI: 6.9-416, p <0.0001).

The EPI was significantly correlated with LVEF (r=0.72, p <0.0001); the lower the LVEF, the lower the EPI. However, patients with similar LVEF had significant variation in their EPI and hence in their apical flow. In patients with LVEF <= 15%, 84.6% had poor apical flow. While 50% of patients with LVEF >15-30% and 30% of patients with LVEF >30-40% had poor apical flow. Almost all patients with LVEF >=55% (25/26 (96.2%) had normal apical flow (EPI >1). (Figure 5). Within the CMP group, 5 (25%) patients had poor apical flow, 3 (60%) had LVEF 10-15% and 2 (40%) had LVEF 30-35%.

When the LVT group was analyzed further, the following was observed: of the 25 patients in the LVT group, 13 (52%) patients had chronic presentation and 12 (48%) patients developed LVT within the first 4 months (range 0-78 days) of their cardiomyopathy diagnosis (acute presentation). Ninety two percent (12/13) % of those with chronic CMP and 83% (10/12) of those with acute cardiomyopathy had EPI <1.0.The ability of the EPI to detect abnormal apical flow in those with LVT therefore did not differ between those with acute or chronic presentation.

Ten out of the 25 patients who had LVT had a prior echo in the preceding 30-723 days. Seventy percent (7/10) of those prior echoes showed EPI of <1.0 and all of them had EPI <=1.2.

Discussion:

This study shows that a low value of the E-wave propagation index is strongly and independently associated with the presence of LVT. In patients with severe cardiomyopathy (LVEF of <40%), an EPI of < 1.0 increased the odd of having LVT by about 30 times compared to patients with EPI of >=1.0. This strong association remained significant even after controlling for LVEF and LVEDV. Furthermore, the presence of an EPI <1.0 on a prior echocardiogram predicts future development of LVT in 70% of the patients. The EPI association with LV presence is significant in both acute and chronic cardiomyopathy conditions.

To our knowledge, this is the first study that describes an easily measured, echocardiographic-based metric that can predict LVT presence in both acute and chronic cardiomyopathic patients. The association of EPI with LVT can be explained by the fact that EPI is a quantitative measurement of the LV apical blood flow. A normal EPI (EPI >1.0) indicates that the mitral jet entering the LV is strong enough to travel the full length of the LV reaching the LV apex, and produce vigorous apical blood flow and apical washout, thereby preventing apical stasis and blood clot formation. E-wave VTI represents the distance the early diastolic wave (E wave) travels inside the left ventricle. In severe cardiomyopathy (acute or chronic) two hemodynamic changes leads to low EPI. The first is reduced E-wave magnitude and duration resulting in a smaller E-wave VTI. This is partly related to reduced stroke volume and cardiac output. The second is dilation and/or elongation of the left ventricle which makes it harder for the E-wave jet to penetrate the full length of the ventricle and to reach the LV apex. The EPI represents a single, distinct metric that incorporates both changes.

Our study data supports the hypothesis that EPI is correlated with LV flow status. Patients with EF >=55% had a very high mean EPI of 1.7 and 96% of them (24 patients) had EPI =>1.2. This strongly suggests that in order to have a normal LV apical flow, there should be a vigorous early

diastolic wave that is able to penetrate the whole length of the LV and wash the LV apex. An E-wave VTI that is larger than the length of the LV length (EPI> 1.0) represents such a wave. In the CMP group, the mean EPI is reduced to 1.2 and 80% of this group (20 patients) had EPI >=1.0. This suggests that the apical flow in the CMP group is reduced compared to the normal LVEF group but is likely adequate to produce sufficient apical washout and prevent apical stasis and LVT development. Based on these findings, we hypothesize that those patients within the CMP group who have an EPI of <1.0 are at high risk of LVT development and might need prophylactic anticoagulation to prevent LVT formation.

The relationship of LV blood flow pattern and development of LVT have been described in prior studies. Van Dantizig et al (8) prospectively evaluated the role of LV flow pattern using echo Doppler in 104 patients who had acute MI. They found that abnormal LV flow measured by echo Doppler was the only independent predictor of LVT development. That study defined two forms of abnormal LV flow patterns: the apical rotating flow and the vortex ring formation. However, their findings could not be applied in everyday clinical practice because of the complexity and the subjectivity of detecting the abnormal flow described in their study which included using color M-mode, color Doppler interpretation and pulse wave Doppler at different locations within the LV cavity. On the other hand, the EPI is very easy to obtain. The E-wave VTI is obtained routinely in every echo examination as part of the diastolic function evaluation. The LV length is easily obtainable from the 4- or 2- chamber view. Our method does not depend on optimal echo images or color Doppler interpretation and does not require any extra images to be added to regular clinical echo protocol. This makes it easy to measure and use by modern-day busy echo labs.

Our study shows that 70% of patients with EPI <1.0 on a prior echo developed LVT subsequently. This is very consistent with findings from other studies. Delamarre et al showed that out of the 10 patients who had persistently abnormal flow pattern at 3 month post MI, 7 (70%) developed LVT, while none of those with normal LV flow patterns developed LVT (7).

Although, EPI and LVEF were significantly correlated, the ability of the EPI to predict the presence of LVT cannot be fully explained by differences in LVEF. When LVEF was controlled in the multivariate model, the association of low EPI and LVT became even stronger. The odds ratio of presence of LVT in those with EPI <1.0 compared to patients with EPI >=1.0 increased from 29.3 to 53.7 ($p < 0.0001$) after controlling for LVEF and LVEDV. The EPI can therefore be used as an adjunct parameter to classify risk of LVT in patients with reduced LVEF given EPI ability to detect apical flow strength in patients with reduced LVEF. For example, 50% of those with LVEF >15-30% had good apical flow and likely to be at low risk of LVT. On the other hand, a significant portion (30%) of patient with LVEF >30-40% had poor apical flow based on EPI and can be at high risk of LVT.

The strong association of EPI with LVT presence was evident in both acute and chronic cardiomyopathy conditions. This is quite important with regard to the pathophysiology of LVT formation. In the acute post MI setting, it is widely believed that myocardial necrosis causes acute inflammation, tissue factor exposure and thrombus formation. That, along with blood stasis from reduced flow, initiates the process of thrombus formation. However, in chronic cardiomyopathy (ischemic or non-ischemic) there is little acute inflammation and blood stasis is the predominant mechanism of LVT formation. It is very likely that blood stasis is a much more important factor in LVT formation than local tissue damage. This is evident from prior studies showing that none of the patients who developed acute Q-wave MI and had a normal LV flow

pattern post MI, developed LVT on follow up (7). Our study supports this notion as it showed that those with EPI>= 1.0 are at much lower odds of having LVT even in acute cardiomyopathy conditions. This supports the notion that the presence of poor apical LV flow is a pre-requisite for LVT development.

The study has multiple potential future clinical implications with regard to anticoagulation therapy whether in acute cardiomyopathy or chronic stable systolic heart failure (HFrEF).

Pending confirmation with prospective studies, the following clinical observations can be drawn from our study: first, the vast majority (85%) of patients with markedly reduced LV systolic function with LVEF of <=15% have poor apical blood flow and at high risk of development LVT; second, EPI can be used in the acute phase of post MI patients as a parameter in addition to LVEF and anteroapical akinesis, to determine the need for anticoagulation therapy for LVT prevention. Third, in patients with chronic severe cardiomyopathy (LVEF < 40%) EPI can be used as an easily-obtained metric to determine the need for anticoagulation LVT formation; and finally, an improving EPI or normalization of the EPI may suggest improvement in apical flow and lower risk of LVT formation which can guide the duration of anticoagulation in primary or secondary prevention of LVT. Further studies are needed to explore the role of EPI on other relevant heart failure outcomes such as stroke, systemic embolization, cardiovascular death or recurrent hospital admissions for decompensated heart failure.

Our study has few limitations. The retrospective nature of the study introduces the risk for selection bias. We used transthoracic echocardiograms to select the CMP group. Compared to cardiac magnetic resonance imaging (MRI), echo has lower sensitivity in detecting small LVT. This might have introduced classification bias by categorizing some of the CMP group as not having LVT. We addressed this partially by individual evaluation of the echo images by the

study team and excluding studies that had suboptimal images where the LV apex was not well seen. We included only cases of definite LVT by echo. The study also excluded patients with very poor pulse wave Doppler signal of the mitral valve. Although our sample size for LVT patients can be considered small, it is quite reasonable considering the low rate of incidence of LVT in contemporary era with aggressive early revascularization and antiplatelet therapy.

Conclusion:

The E-wave propagation index is a novel, easily-obtainable, independent echocardiographic-based metric to evaluate apical LV flow in both acute and chronic cardiomyopathy. An EPI of less than 1 is highly suggestive of poor apical LV flow and indicates a high risk for LVT development. Among patients with LVEF<40%, an EPI of less than 1 increased the odd of LVT by 53.7 times controlling for LV size and systolic function. Prospective studies are needed to validate the use of EPI in anticoagulation therapeutic decisions in patients with cardiomyopathy.

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Figures

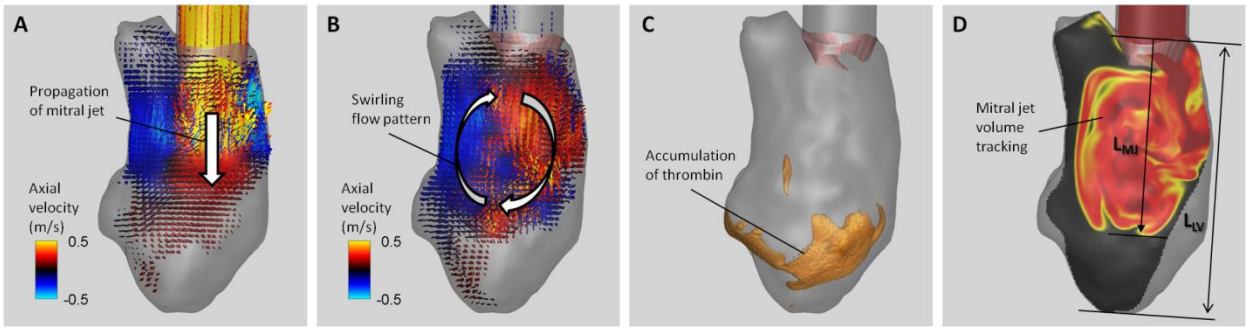

Figure (1): (A) Blood flow in early diastole (E-wave). (B) blood flow in later diastole showing swirling of blood flow inside the LV. (C) High thrombin concentration in the apical region where blood flow velocities are reduced. (D) Mitral jet volume in early diastole fails to reach the LV apex for this patient. The distance traveled by the E-wave is shorter than the length of the LV indicating poor apical washout.

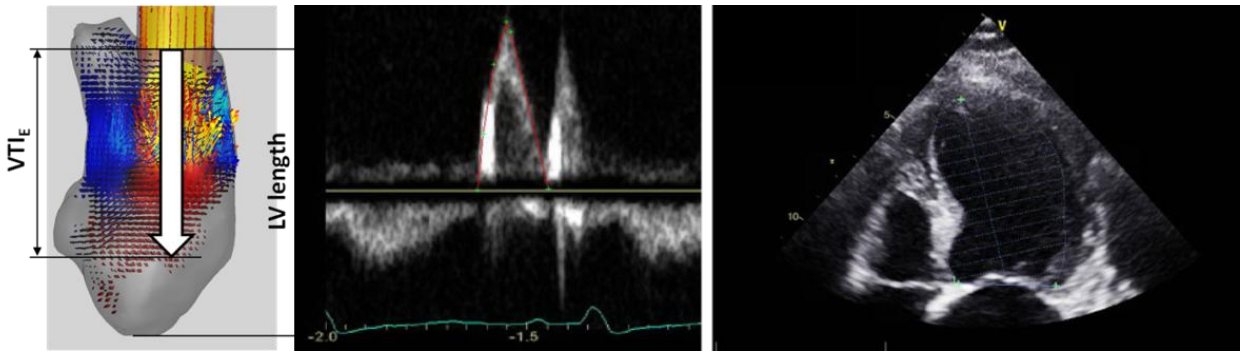

Figure 2: Measurement of E-wave propagation index (EPI). Velocity time integral of the E-wave as measured from pulse Doppler at the mitral valve leaflet tips. The LV length at end diastole as measured from the apical 4-chamber view of transthoracic echo. EPI = E-wave VTI/LV length.

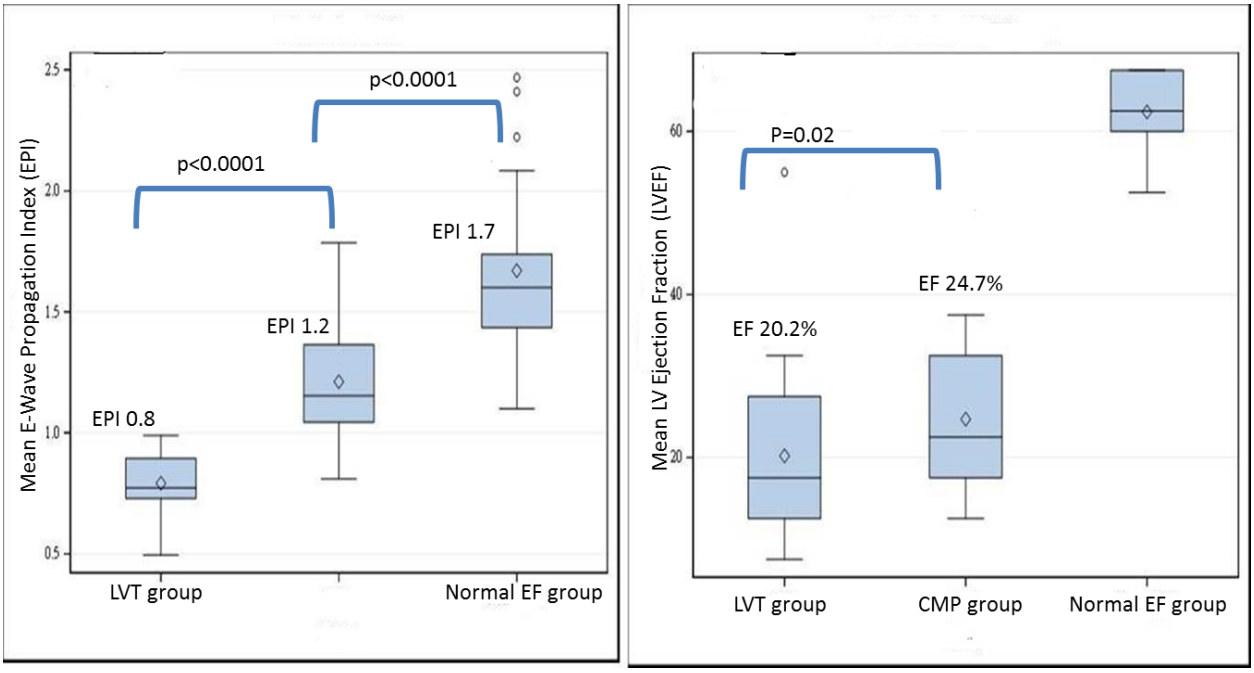

Figure 3A: Distribution of mean EPI among the 3 study populations. EPI is significantly lowest in those with LVT compared to those with cardiomyopathy and those with normal LV ejection fraction.

Figure 3B: Distribution of the mean LVEF among the 3 study populations. LVEF is slightly, but significantly lower in the LVT group compared to the cardiomyopathy group.

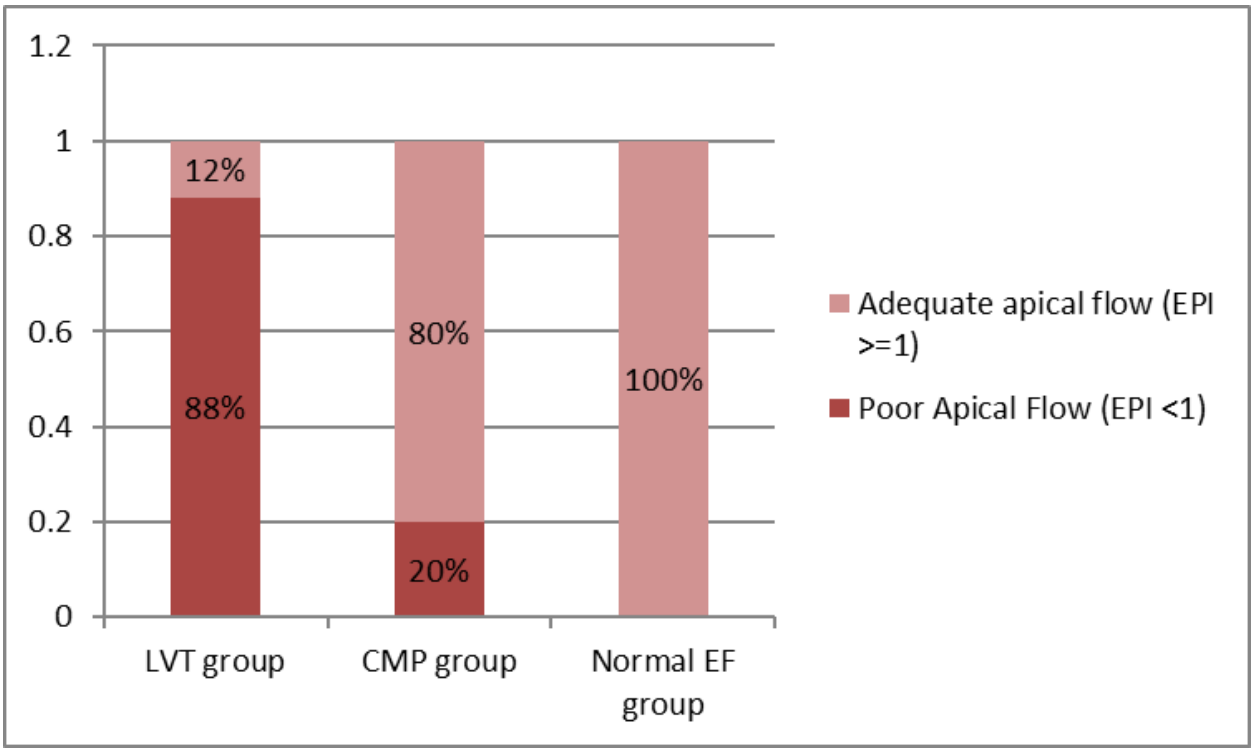

Figure 4: Distribution of patients who has poor apical blood flow as measured by EPI <1.0 among the 3 study populations. EPI: E-wave propagation index; LVT: left ventricular thrombus: CMP: Cardiomyopathy; EF: ejection fraction

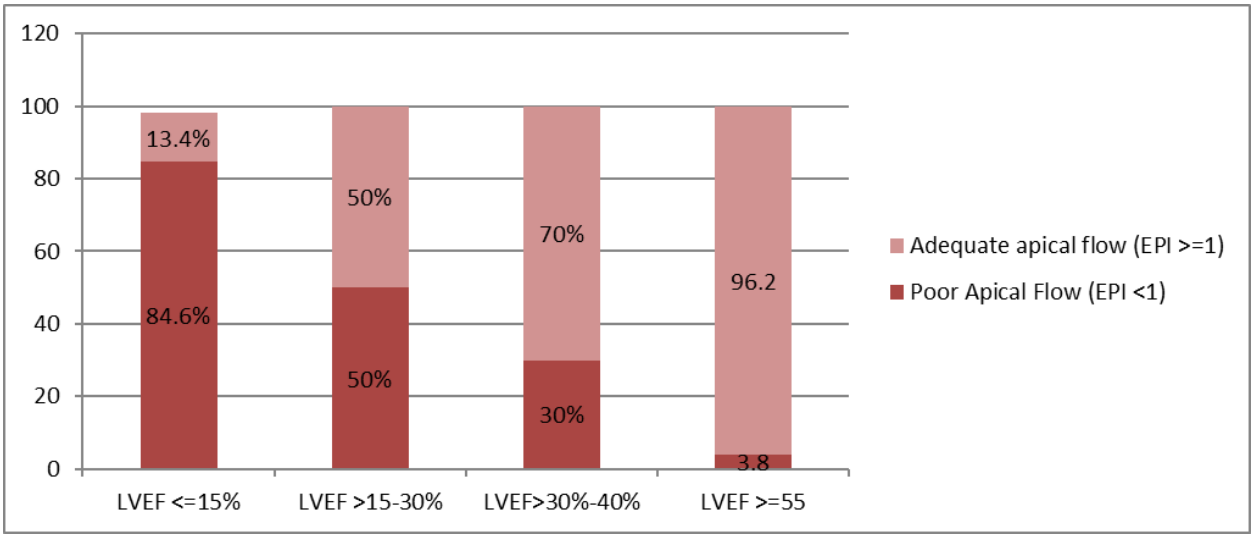

Figure 5: Distribution of patients with poor apical blood flow as measured by EPI <1.0 by LVEF.

EPI: E-wave propagation index; LVEF: left ventricle ejection fraction

Supplementary video 1: Computational fluid dynamic modeling -derived, coupled chemical and hemodynamic profile of patient with history of Left ventricular thrombus. It shows that the early diastolic flow does not reach the apex resulting in high thrombin concentration.

Supplementary video 2: Computational fluid dynamic modeling -derived, coupled chemical and hemodynamic profile of patient with history of Left ventricular thrombus. It shows that the early diastolic flow does not reach the apex resulting in high thrombin concentration.

Supplementary video 3: Computational fluid dynamic modeling -derived, coupled chemical and hemodynamic profile of patient with history of Left ventricular thrombus. It shows that the early diastolic flow reaches the apex resulting in an improved apical flow and lower thrombin concentration.

Table(1)

Table 1: Characteristics of the study population for categorical variables								
	LVT		CMP		Normal		Difference among the 3 groups	Test of difference between the LVT&CMP groups
	N	**%**	**N**	**%**	**N**	**%**	**p-value***	**p-value***
Male Gender	**19**	**76**	**19**	**76**	**12**	**48**	**0.07**	**0.99**
Hypertension	**14**	**56**	**20**	**80**	**12**	**48**	**0.05**	**0.13**
Diabetes Mellitus	**11**	**44**	**9**	**36**	**8**	**32**	**0.76**	**0.77**
Smoking active	**6**	**24**	**1**	**4**	**2**	**8**	**0.13**	**0.1**
Prior Myocardial infarction	**14**	**56**	**7**	**28**	**0**	**0**	**NA**	**0.08**
Ischemic CMP	**14**	**56**	**9**	**36**	**0**	**0**	**NA**	**0.26**
E-wave Propagation Index<1	**22**	**88**	**5**	**20**	**0**	**0**	**<0.0001**	**<0.0001**

*** Fisher exact test**
NA: Not applicable
CMP: cardiomyopathy

Table(2)

Table 2: Characteristics of the study population for continuous variables

	LVT		CMP		Normal		Difference among the 3 groups	Test of difference between the LVT&CMP groups
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**	**p-value****	**p-value***
Age (year)	**55.1**	**15.4**	**61.3**	**16**	**56.7**	**16.4**	**0.15**	**0.05**
BMI (kg/m^2)	**27.5**	**6.7**	**28.1**	**3.1**	**26.6**	**6.5**	**0.1**	**0.29**
LVEF (%)	**20.2**	**10.4**	**24.7**	**8**	**62.4**	**4.3**	**<0.0001**	***0.02**
Heart rate (beats per minute)	**82.7**	**17.2**	**78.5**	**24.7**	**67.8**	**11.6**	**0.02**	***0.01**
Stroke volume (ml)	**43.7**	**14.2**	**59.7**	**21.6**	**81.2**	**30.6**	**<0.0001**	***0.01**
LVEDV (ml)	**179.5**	**55.9**	**164.4**	**63.4**	**90.4**	**27.6**	**<0.0001**	**0.2**
LV length (cm)	**9.9**	**0.8**	**9.5**	**1**	**8.5**	**0.8**	**<0.0001**	**0.13**
E-wave peak velocity (cm/second)	**68**	**16.3**	**84.6**	**24.3**	**84.5**	**18.4**	**0.003**	**0.009**
E-wave VTI (cm)	**7.8**	**1.4**	**11.4**	**2.6**	**14.1**	**2.9**	**<0.0001**	**<0.0001**
E-Wave Propagation Index	**0.8**	**0.14**	**1.2**	**0.3**	**1.7**	**0.3**	**<0.0001**	**<0.0001**

**** Kruskal_Wallis test**

***Mann-Whitney test**

LVEDV: left ventricular end diastolic volume, LV length: Left ventricular length

Video (1)

Click here to download Video Still: supp_video_1_LVT01(H264)_.mp4

Video (2)

Click here to download Video Still: supp_video_2_LVT02(H264).mp4

Video (3)

Click here to download Video Still: supp_video_3_LVT09(H264).mp4