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Current Clinical Application of Intracardiac Flow Analysis Using Echocardiography

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In evaluating the cardiac function, it is important to have a comprehensive assessment of structural factors, such as the myocardial or valvular function and intracardiac flow dynamics that pass the heart. Vortex flow that form during left ventricular filling have specific geometry and anatomical location that are critical determinants of directed blood flow during ejection. The formation of abnormal vortices relates to the abnormal cardiac function. Therefore, vortex flow may offer a novel index of cardiac dysfunction. Intracardiac flow visualization using ultrasound technique has definite advantages with a higher temporal resolution and availability in real time clinical setting. Vector flow mapping based on color-Doppler and contrast echocardiography using particle image velocimetry is currently being used for visualizing the intracardiac flow. The purpose of this review is to provide readers with an update on the current method for analyzing intracardiac flow using echocardiography and its clinical applications.

KEY WORDS: Intracardiac flow · Vortex · Echocardiography · Particle image velocimetry.

Introduction

With the development of new cardiovascular imaging technology, it is now possible to precisely analyze the structure and function of the heart. However, we are still frequently met with discrepancies between patient's symptoms and imaging results. Interest in intracardiac flow analysis has been gradually increasing in recent years. In evaluating the cardiac function, it is important to have a comprehensive assessment of structural factors, such as the myocardial or valvular function and intracardiac flow dynamics that pass the heart. Intracardiac flow analysis can have an important incremental value over conventional cardiovascular imaging modalities including echocardiography, cardiac computed tomography, and magnetic resonance imaging (MRI) in the assessment of patients in the very early stage of cardiovascular disease or complex geometry after cardiac surgery. This has become possible due to the development of new technologies in cardiovascular imaging, which expand our options to visualize and analyze the complex intracardiac flow and use its information in the evaluation of cardiac function. In this review, we will describe the details of the current method for analyzing intracardiac flow as well as its clinical applications.

Intracardiac Flow and Cardiac Vortex

The bloods flow through the heart is closely associated with intracardiac structures such as the myocardium, valves and large vessels around the heart.[1)] In response to the structural and functional changes in the heart, this intracardiac blood flow should be changed accordingly, thereby, optimizing the intracardiac blood flow to preserve efficient cardiac output. There is an intimate relationship between the intracardiac flow and cardiac function; detection of the early changes of the intracardiac flow is crucial in diagnosing very early stages of cardiac disease, as well as in the prediction of prognosis.[2)]

A vortex can be described as a fluid structure that possesses circular or swirling motion spinning around a virtual central axis. Vortices that form during left ventricular (LV) filling have specific geometry and anatomical location that are criti-

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cal determinants of directed blood flow during ejection.[3)4)] The formation of abnormal vortices also relates to the abnormal cardiac function.[5)6)] Therefore, vortex flow may offer a novel index of cardiac dysfunction.[2)7)] However, visualizing and measuring intracardiac vortex flow is not simple due to several technical problems. Recent technological innovations in imaging modalities and the emergence of flow visualization techniques have provided valuable opportunities for direct *in vivo* assessment of multidirectional blood flow in the heart.[1)]

Several pioneering studies have demonstrated that the role of vortex in the heart might be to 1) prevent collision of flow, 2) preserve kinetic energy (KE) and avoid excessive dissipation of energy, 3) redirect and sling blood towards left ventricular outflow tract, and 4) enhance reciprocation of atrial and ventricular function.[3)4)] These flow patterns in the heart have shown differences related to various factors including age, gender, blood pressure, and ventricular geometry and function.[8)9)]

Methods for Visualization of Intracardiac Flow

Cardiac magnetic resonance (CMR) and echocardiography have been used for non-invasive analysis of intra-cardiac blood flow pattern. Table 1 comprises a list of the advantages and disadvantages of each method.

Cardiac MRI

Velocity encoded phase contrast (PC)-CMR is the most frequently used CMR technique for acquiring blood flow in the cardiac chambers and major vessels.[10-12)] Although real-time PC-CMR is possible for 2-dimensional (2D) measurements, better quality data can be obtained by combining the information from several heartbeats using electrocardiogram (ECG) gating.[1-12)] The acquired 2D PC-CMR data can be used for flow quantification which enables the calculations of flow-time curves, net flow, mean velocities, peak velocities, and retrograde fraction.[13)] Currently, via ECG and respiratory gating, the complete time-resolved, 3-dimensional (3D), and 3-directional velocity field can be measured over a volume that covers the complete heart or large vessels.[14)15)] This 3D cine phase-contrast CMR technique enables the measurement of the intracardiac blood flow with a higher resolution and a shorter acquisition time (Fig. 1).[1)] To visualize complex, three-directional blood flow within a 3D volume, various visualization tools, including 2D vector-fields, 3D streamlines, and time-resolved 3D particle traces have been proposed.[13)16)17)] Limitations associated with CMR flow visualization are the as follows: 1) generation of flow information from averaged flow values over several cardiac cycles,[13)] 2) its lower temporal resolution, 3) not applicable at bedside, 4) a longer test duration, and 5) a rather high cost[18)19)] for use in daily clinical practice.

Echocardiography

Intracardiac flow visualization using ultrasound technique has definite advantages with a relatively lower cost, shorter post-processing time, higher temporal resolution and availability in real time clinical setting.[1)13)] Vector flow mapping (VFM) based on color-Doppler and contrast echocardiography (CE) using particle image velocimetry (PIV) is currently being used for visualizing the intracardiac flow using ultrasound.

Color-Doppler based flow analysis

Color-Doppler technique is simple, reliable method to visualize intracardiac unidirectional flow along the line of each ultrasound beam.[2)] VFM technique, based on color-Doppler data has recently been developed and has shown reasonable accuracy[20)] both *in vitro* and *in vivo* settings (Fig. 2).[21)] VFM solves angle-dependency problem through mathematical calculations based on echo-dynamography.[1)] This consists of a series of

Table 1. Comparison of intracardiac flow visualization methods

	CE-PIV	Color Doppler-VFM	Phase contrast- CMR
Signal source	Tracking of contrast microbubbles	Color Doppler based flow mapping	Velocity encoded phase contrast MRI
Resolution	Good spatial resolution in 2D, limited 3D	Good spatial resolution in 2D and 3D	Good spatial resolution in 2D and 3D
Advantages	1) Bedside, lower cost, short process time	1) Bedside, lower cost, short process time	1) Unrestricted access
	2) Accurate visualized vortex	2) Do not require contrast microbubbles	2) Full 3D capability
	3) Validated quantitative parameters		
Limitations	1) Need contrast agent	1) Lacking validated parameters	1) Need several cardiac cycles
	2) Need higher frame rate	2) Need manual de-aliasing	2) Longer examination time
	3) Acoustic windows	3) Lower temporal resolution	
Accuracy	1) Limited in high velocity flow	1) Accurate in high velocity	1) Accurate in high & low velocity
	2) Accurate in low velocity flow	2) Underestimation in low velocity	
Applications	1) Measure for LV, RV function	1) LV function analysis	1) Measurement of flow in cardiac chambers & aorta
	2) LA, aorta flow	2) Valve function analysis	

CE-PIV: contrast echocardiography-particle image velocimetry, VFM: vector flow mapping, CMR: cardiac magnetic resonance, 2D: 2-dimensional, 3D: 3-dimensional, MRI: magnetic resonance imaging, LV: left ventricle, RV: right ventricle, LA: left atrium

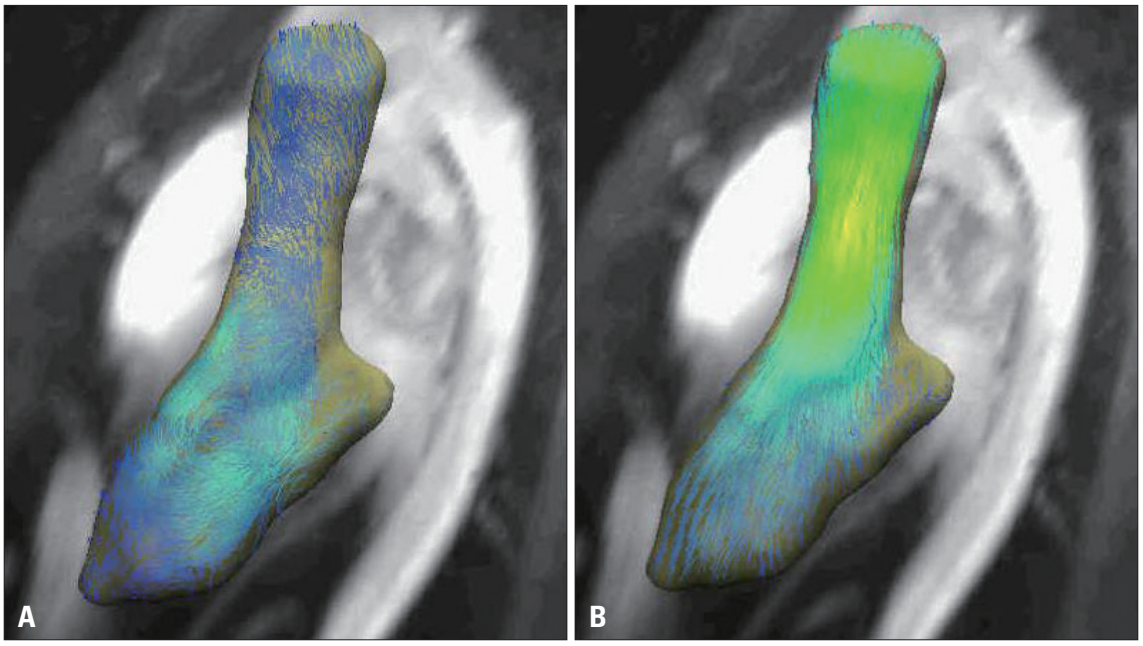

Fig. 1. Four-dimensional flow magnetic resonance imaging (MRI) and visualization of 3-dimensional flow. Four-dimensional cine MRI views of left ventricle and ascending aorta in normal subject in diastole (A) and systole (B).

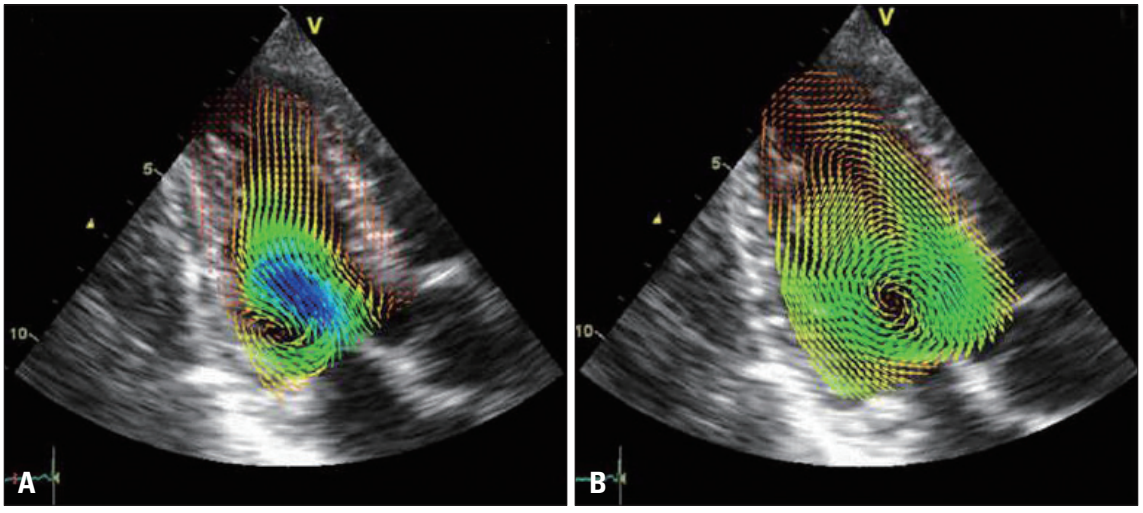

Fig. 2. Examples of blood velocity mapping in a normal left ventricle overlaid on a sequence of anatomical B-mode apical long-axis images during early diastole (A), isovolumic contraction (B). Redrawn from Garcia et al.[21]

equations aimed at converting a 2D distribution of measured axial velocities (parallel to the ultrasound beam) and estimated radial velocities (perpendicular to the former ones) into a plane of vortical and nonvortical flow vectors.[22] However, color-Doppler derived flow method has several limitations to note: 1) lower temporal and spatial resolution; 2) underestimation of low velocity flow; and 3) the need for de-aliasing process.

CE-PIV TECHNIQUE

Vorticity imaging by CE using PIV (CE-PIV) is a novel approach to visualize the intracardiac flow. Recent advances in contrast media and ultrasound tissue harmonic imaging techniques have made it possible to visualize and record the movements of single microbubbles in the cardiac chambers (Fig. 3).[2] To this extent, CE may be a better and more convenient modality to investigate the complex flow field in the heart.[23][24] PIV is an optical method used to measure velocities and related properties in fluids.[25] The fluid is seeded with particles, which, for the purposes of PIV, are generally assumed to faithfully follow the flow dynamics. It is the motion of these seeding particles that is used to calculate information on velocity.[25][26] Using PIV, velocity is estimated on the basis of displacement of contrast bubbles. From the whole velocity vector, the vorticity-the curl of velocity-is computed. The CE-PIV technique is noninvasive, and its latest developments allow a high degree of accuracy[25-27] both *in vitro*,[28] and *in vivo* settings.[2] However,

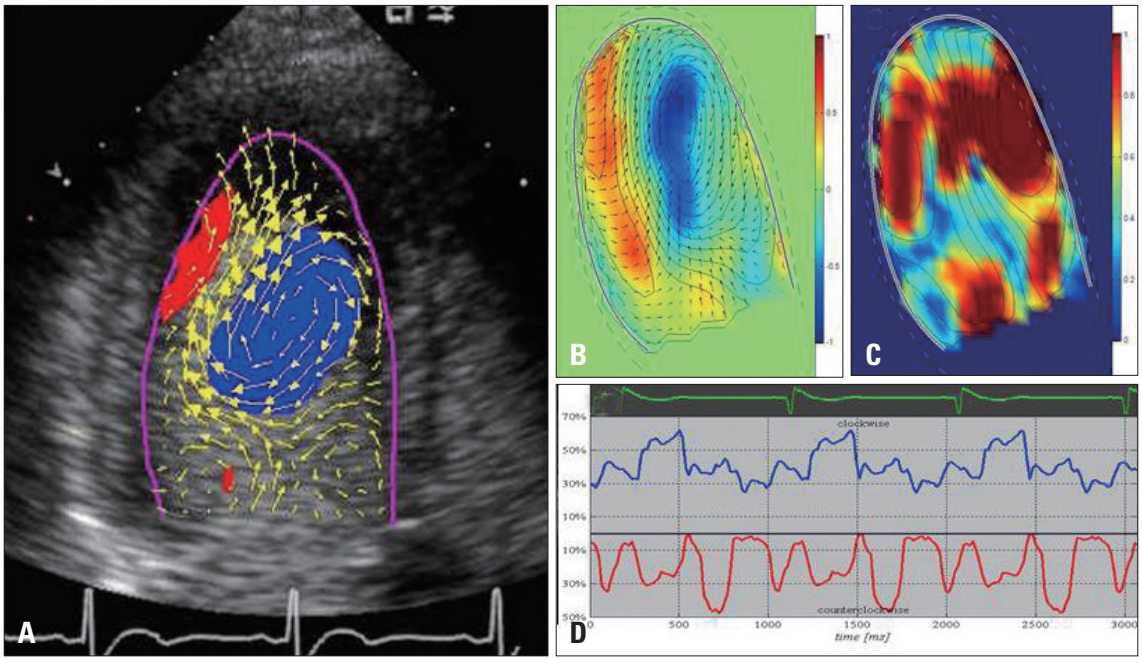

Fig. 3. Example of left ventricular vortex flow analyzed by contrast echocardiography using particle image velocimetry method. The echo freeze frames represent the velocity vector on the scan-plane, superimposed to the reconstructed Doppler representation (A). Parametric representations of steady streaming field (B), pulsatile strength field (C) and vortex size change throughout the cardiac cycle (D). Redrawn from Hong et al.[2]

Table 2. Quantitative parameters and clinical applications of intracardiac flow analysis

Area	Clinical application	Disease	Parameters	Technique
LV function	Systolic function	Heart failure, DCMP	VD, VW, SI, RS, VFT, KED index	CE-PIV, VFM
	Diastolic function	HFNEF, RCMP	RS, Min-VS, VFT	CE-PIV, VFM
	Apical thrombus	AMI, DCMP	VD, RS	CE-PIV
	LV dyssynchrony	DCMP	Vortex intensity, VFT	CE-PIV, VFM
LA function	Treatment strategy	AF	Vortex location, VRS	CE-PIV, CMR
	LA thrombus	AF, VHD	Vortex location, intensity	CE-PIV, CMR
RV function	RV systolic function	PAH, CHD, PTE	Vortex location, intensity	CE-PIV, CMR
Valve disease	Valvular function	VHD		CMR, VFM
	Prosthetic valve	VHD		CE-PIV, VFM
	LV remodeling after valve surgery	DCMP, VHD	Vortex location, intensity	CE-PIV, CMR
Aorta	Shear stress	Aortic dissection, CoA	KE, shear stress	CMR
	Aortic atherosclerosis	HTN, dyslipidemia	Shear stress, vortex intensity	CE-PIV, CMR
	Risk of aortic dilation	Marfan SD, bicuspid AV	Shear stress	CMR
	Vasculo-ventricular coupling	HTN	Vortex intensity	CE-PIV, CMR

LV: left ventricle, LA: left atrium, RV: right ventricle, DCMP: dilated cardiomyopathy, HFNEF: heart failure normal ejection fraction, RCMP: restrictive cardiomyopathy, AMI: acute myocardial infarction, AF: atrial fibrillation, VHD: valvular heart disease, PAH: pulmonary arterial hypertension, CHD: congenital heart disease, PTE: pulmonary thromboembolism, CoA: coarctation of aorta, HTN: hypertension, SD: syndrome, AV: aortic valve, VD: vortex depth, VW: vortex width, SI: sphericity index, RS: relative strength, VFT: vortex formation time, KED: kinetic energy dissipation, Min-VS: minimal vortex size, VRS: vortex relative strength, KE: kinetic energy, CE-PIV: contrast echocardiography-particle image velocimetry, VFM: vector flow mapping, CMR: cardiac magnetic resonance

several limitations exist in the detection of high velocities due to the need for very high frame rates and microbubbles.

CLINICAL APPLICATION OF INTRACARDIAC FLOW ANALYSIS

There are growing interests in the clinical applications of intracardiac flow analysis using various techniques. Although, CMR and VFM have offered qualitative vortex flow parameters, CE-PIV have suggested several reliable quantitative parameters. Table 2 is comprised of a list of the current available quantitative parameters for evaluating cardiac function and proposed clinical application of intracardiac vortex flow analysis.

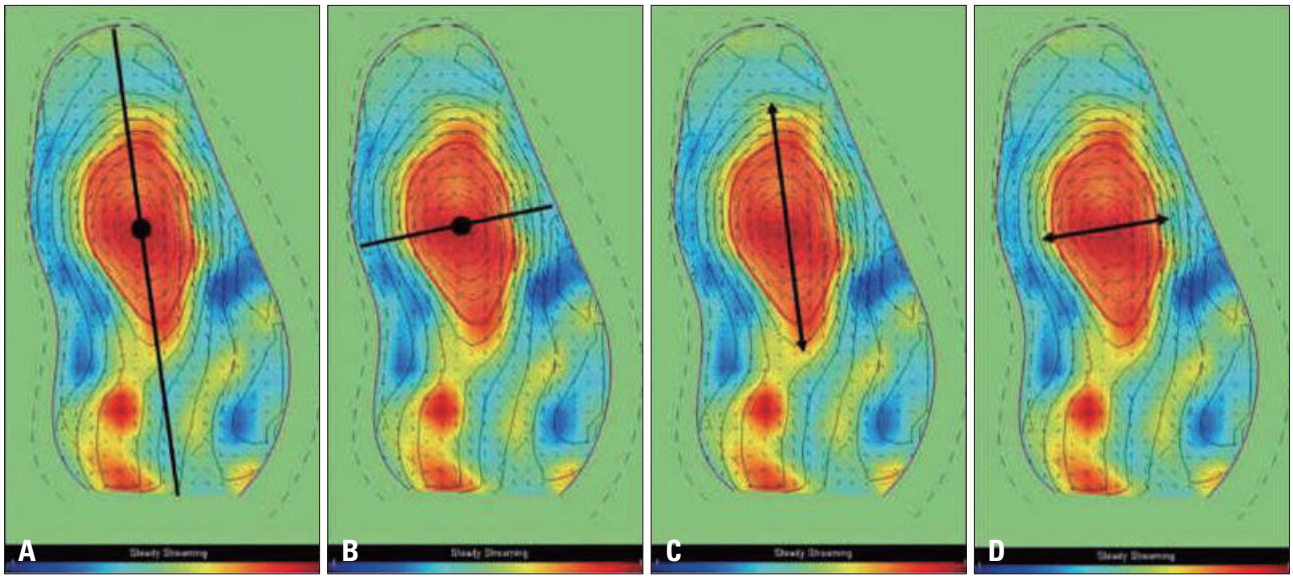

Fig. 4. Description of quantitative parameters of the vortex location and shape. Vortex depth (A, black line), vortex transverse position (B, black line), vortex length (C, black arrow), and vortex width (D, black arrow). Redrawn from Son et al.[30]

QUANTITATIVE PARAMETERS FOR LEFT VENTRICULAR VORTEX FLOW

In normal subjects, after ejection, the direction of flow reversed towards the apex with a brief appearance of vortex at the early stage of isovolumic relaxation time. The major diastolic anterior vortex developed immediately after the onset of the early diastolic phase. This vortex continued during diastasis, and persisted into late LV filling phase. This vortex also persisted throughout isovolumic contraction time and dissipated with the opening of the aortic valve and LV ejection.[2] Recent studies have suggested several quantitative parameters for defining properties of vortex including vortex location, morphology, pulsatility, vortex formation time (VFT),[22] and KE.[29]

VORTEX LOCATION

For the evaluation of the location of vortex, vortex depth (VD) and vortex transversal position (VT) have been proposed. VD represents the vertical position of the center of vortex relative to the LV long axis, and VT represents the transverse position relative to the posteroseptal axis (Fig. 4).[2][30] In patients with acute anterior wall myocardial infarction who have an apical akinesis or dyskinesis, lower VD (cut off value: 0.45) showed significantly higher incidence of apical thrombus formation (Fig. 5).[30] Therefore preservation of apical vortex is crucial for preventing apical thrombus formation in patients who have an apical akinesis or dyskinesis. Other studies have shown that the location, and duration of vortex flow were markedly altered in patients with systolic dysfunction.[7][9]

VORTEX MORPHOLOGY

Vortex length (VL), width (VW) and sphericity index (SI) are quantitative parameters for depicting the morphology of main

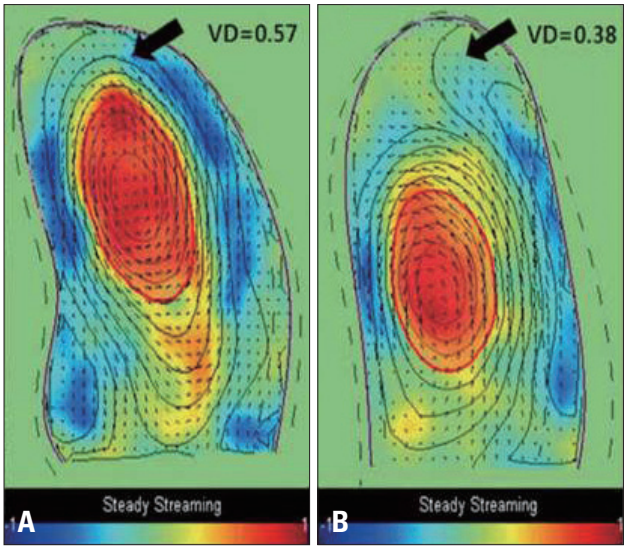

Fig. 5. Parametric representation of the steady streaming field in the non-thrombus (A) and thrombus group (B) are evaluated in apical 4-chamber view. The center of the average vortex flow was located near the apex in the non-thrombus group (A). However, in the thrombus group, the vortex was located in the center of the left ventricle (LV), much farther from the apex and did not reach to the LV apex (B). A black arrow indicates different vortex flow pattern in the apex between the 2 groups. Redrawn from Son et al.[30] VD: vortex depth.

LV vortex. VL can be measured by the longitudinal length of vortex relative to LV length, and VW can be measured by the horizontal length of vortex relative to LV length. SI can be calculated by ratio of VL to VW.[2] Vortex morphology showed dynamic variations during cardiac cycles. Several studies have shown that vortex size and shape (depth, length, width, area, and SI) seem to be associated with LV systolic and diastolic functions,[2] especially in specific moments during the cardiac cycle, such as during isovolumetric contraction or diastasis.[31]

PULSATILE INTENSITY OF VORTEX

For the evaluation of pulsatility of LV vortex, 3 pulsatility parameters including relative strength (RS), vortex relative strength (VRS), and vortex pulsation correlation (VPC) of LV vortex have been proposed. The RS represents the strength of the pulsatile component of vorticity with respect to the average vorticity in the whole LV. The VRS represents the same ratio accounting for the pulsatile vorticity of only the vortex, instead of the entire LV. The VPC is the correlation between the steady and pulsatile vorticity in the vortex, normalized with the vortex strength and area to make a dimensionless parameter.[2] In the various clinical settings, vortex pulsatility intensity is lower in patients with symptomatic, systolic or diastolic dysfunctions.[2)31)32]

VORTEX FORMATION TIME

VFT, a dimensionless parameter representing the duration of early diastole and hence, reflecting the quality of ventricular filling, is correlated with transmitral thrust and mitral annulus recoil. Therefore, VFT is considered to be a powerful tool in assessing diastolic performance.[33-35] The VFT index has already demonstrated its applicability in detecting alterations in transmitral flow efficiency and its association with the prognosis of heart failure patients.[36]

ENERGY PARAMETERS

Energy loss index can be measured by both VFM and CE-PIV. However, only CE-PIV has data comparing normal subjects with patients with dilated cardiomyopathy. KE dissipation measures the amount of energy, ΔKE, that is dissipated into the heart during the phases of the cardiac cycle, and it can be calculated from the time integral of the rate of KE dissipation.[4)37] In patients with reduced cardiac output, KE dissipation index is significantly higher compared with normal control.[38]

LEFT ATRIAL VORTEX FLOW ANALYSIS

Although conventional Doppler echocardiography is the most widely used and a simple diagnostic tool to evaluate the left atrial (LA) function[39] and to identify those at high risk for thromboembolic events[40] in daily practice, it has several limitations in the assessment of early hemodynamic changes of the LA and prediction of thromboembolic risk in patients with atrial fibrillation (AF). Thus, characterization and quantification of the LA flow pattern has the potential benefit of estimating LA function and predicting thromboembolic events in patients with AF. LA vortex flow analysis using PC-CMR and transesophageal CE-PIV (Fig. 6) is feasible to characterize and quantify the LA vortex flow.[41)42]

OTHERS

Clinical applications of CE-PIV have been reported in various clinical settings, including in detecting of areas of with a risk of potential apical thrombus formation due to absence of vortex flow,[30] analyzing right venricular flow,[29] and identify-

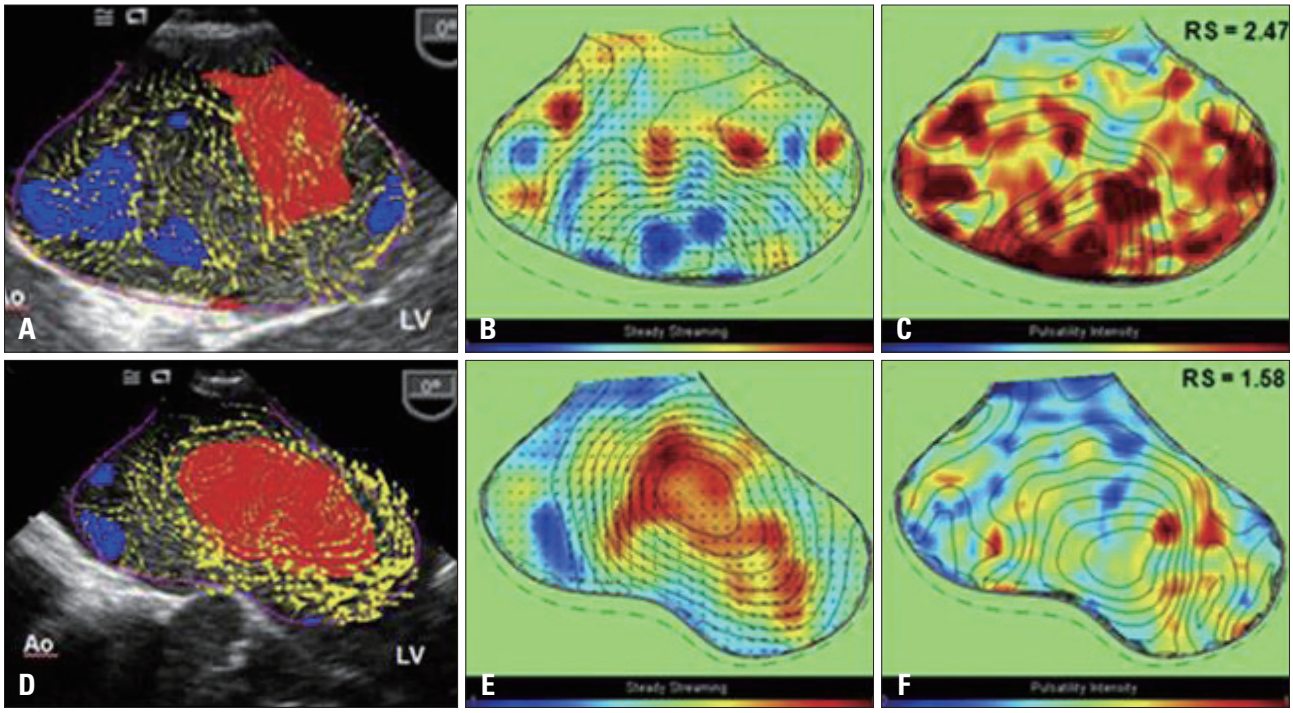

Fig. 6. The echo freeze frames (A and D) parametric representation of steady streaming field (B and E) and the pulsatile strength field (C and F) in the control group (upper panel) and the atrial fibrillation (AF) group (lower panel). The left atrial flow in controls showed several vortices with strong pulsatility in the periphery (B and C, red-colored area), whereas a large, merged, and spherical vortex with weak pulsatility (E and F, blue-colored area) was noted in the AF group. Redrawn from Park et al.[42] Ao: aorta, LV: left ventricle, RS: relative strength.

ing changes in flow motion in paced rhythms.[43] Several groups have attempted to make advancements in the analysis of blood flow through prosthetic valves, effect of vortex flow in obstructive hypertrophic cardiomyopathy, blood flow characteristics in the thoracic aorta, and cardiac resynchronization therapy.[44][45]

Summary and Conclusions

With advancing new technology, it is possible to analyze not only the structural function of the heart but also the intracardiac flow by non-invasive cardiac imaging modalities with reasonable accuracy. Using CE-PIV and color-Doppler derived VFM, the intraventricular vortex flow has been successfully demonstrated, validated and has been made applicable in some clinical settings. Therefore, comprehensive assessment of intracardiac structure and vortex flow may enable the detection of pathologically altered flow characteristics and identification of new pathophysiologic mechanisms in the development of cardiac and vascular disease. Further improvement of this novel technology may lead us to obtain additional information on hemodynamics and has the potential for early detection of the cardiac dysfunction and application for decision-making regarding treatment strategy in various clinical settings.

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