Heart failure is diverse in its manifestations and pathophysiology with changes in chamber size and volume, wall motion, valvular competence, intracardiac pressures, and electrical events. These are routinely measured with well-established methods. However, it is common to observe different degrees of compensation despite echocardiographically similar degrees of cardiac dysfunction. How can we explain this phenomenon? One persistent gap in our understanding of the failing heart is the global behavior of the intracardiac blood flow and its potential impact on pump efficiency and disease progression. The concepts that ventricular filling and ejection are separate events distinct in timing and location and that acceleration and ejection of the stroke volume are only events due to systolic myocardial contraction are familiar but likely oversimplified. It seems reasonable that rather than coming to a halt at end diastole, flowing blood would keep moving as filling transitions to ejection and that it would be efficient for blood in the end-diastolic left ventricle (LV) to already be moving toward the aortic valve for ejection. Until recently, there was a lack of measurement tools able to accurately resolve the complex in vivo 3D flow fields to investigate these and other flow-based questions. New tools that can measure 3D flow throughout the cardiac cycle noninvasively are becoming increasingly mature, and a more detailed perspective is emerging on the organization of intracardiac flow.

Accurately Measuring 3D Flow Patterns in the Beating Heart

To study flow in the failing heart, we must first understand the process in health. It can be hypothesized that the normally functioning LV will have a consistent and efficient pattern of throughflow, which represents a balance of hemodynamic conditions, chamber configuration, and rhythm. Proving this hypothesis requires an accurate way of measuring and interpreting dynamic flow in the heart.

Flow passes through the LV cavity without constraint to any single plane or predefined direction; therefore, the necessary tools used in this task must be accurate in measuring blood flow velocities irrespective of direction in 3 spatial dimensions (3D) and with registration to time throughout the phases of the cardiac cycle. Previous assumptions about intracardiac flow have been shaped by the limitations of our more familiar tools such as spectral and color Doppler, which measure a single velocity component and lose the true flow velocity rather than demonstrate that the flow path is veering away from the axis of the beam. Three-dimensional reconstructions of slices with this single-directional velocity will not overcome these limitations. Recent advances in inherently multidimensional methods, as opposed to the more familiar 3D reconstructions of non-3D measurements, have been a critical step that has empowered new insights into intracardiac flow.

A more promising method is phase-contrast MRI. This widely available tool is able to measure velocities that are accurate in 3 directions. It can be used to acquire a time-resolved, 3D set of data that includes the blood flow velocities throughout the entire heart and other vascular structures over an averaged cardiac cycle. Because these data are taken from many heart beats, flow instability or beat-to-beat fluctuations will not be apparent. Multidimensional images of the average flow behavior have been applied to investigations of the normal and aneurysmal aorta, aortic coarctation, the heart in normal and heart failure states, and the cerebrovascular circulation.

Visualization of these data can be complex but is critical to their interpretation. Particle tracing is a method that visualizes flow by emitting virtual particles at a specific
region and time in the flow field. The particles can be used to get a snapshot of the velocity field at a specific time by creating streamlines; following the particles in the flowing blood over time creates an image with pathlines that demonstrate the routes through the heart. This approach to flow visualization has allowed intuitive visualizations and quantification of the flow throughout the cardiovascular chambers in a way that has not been previously accessible. These methods have limitations that stem from their limited spatial and temporal resolution, which make them insensitive to mixing and rapid or small flow events and incremental errors that accumulate if pathlines are followed too long. However, these limitations are unlikely to distract from the global, averaged flow behaviors that are studied with these methods. Other MRI-based flow investigations of the cardiovascular system are being developed to address function in different ways and are contributing to flow-based study of ventricular function.

Flow in the Normal LV: The Surprise Inside

The blood flow inside the normal LV is dynamically arranged with regions of straight and turning flow, flow-flow interactions, recirculating masses of blood, and vortices that develop and extinguish with the phases of the cardiac cycle.17–20 Hints of these structures come to us from studies performed with methods such as contrast,21–22 Doppler,5 and particle velocimetry.23 These flow structures can be detected in planes through the heart (Figure 1; supplemental Video I), including the variable size and positions of vortical flow24 that in normal hearts is initiated early in diastole underneath the mitral valve leaflets and reaccelerates during atrial contraction.

Using analysis methods based on particle trace techniques, the normal ventricular blood volume has been divided into 4 components according to different behaviors over the cardiac cycle (Figure 2; supplemental Video II).4 The total inflow to the LV during diastole is divided between direct inflow, which enters and exits the LV in 1 beat, and retained inflow, which enters the LV but is not ejected with the next systole (Figure 3). There is also a volume that is already within the LV at the onset of diastole but achieves ejection during the ensuing systole (the delayed ejection volume). Finally, there is a residual volume that both starts and ends the cardiac cycle in the failing heart. This concept of a relatively efficient route through the LV would imply a relatively smooth course with a short distance from inflow to outflow. Even if the amount of momentum preserved in this way is small, there might be other consequences of failing to preserve it. Kinetic energy lost in deceleration would convert to heat or pressure; preserving some portion of inflow kinetic energy might allow the heart to function at lower diastolic pressure than otherwise.

The route followed by the direct flow is like a chute through the LV. The boundaries of this pathway are not shaped by anatomic structures but rather by the interaction with the other flow components, which define the route for direct flow and create the vortical flow structures below the mitral valve leaflets. The characteristic distribution and proportions of these components have been shown in early work to be relatively consistent in normal ventricles across a spectrum of heart rates and ages.4 Newer, more accurate methods estimate that the direct flow is more than one third of the end-diastolic volume in normal hearts.25

Figure 1. Flow throughout the LV is shown in an apical 3-chamber plane for a subject with a normal heart (top) and a patient with moderate heart failure (bottom). Flow velocities are demonstrated with streamlines colored corresponding to the flow velocities for early diastole (left), late diastole (middle), and mid systole (right). The cores of flow vortices are indicated by the white structures. In early diastole in the normal heart, a vortex is seen surrounding the peak inflow on the ventricular surfaces of the mitral leaflets. At end diastole, distinct vortices are seen near the mitral valve and in the apical ventricle, and all flow in the outflow tract is moving toward the aortic valve (white arrow). At mid systole, there is concordant ejection of the ventricular flow and extinction of the ventricular vortices. In early diastole in the failing heart, a vortex is seen surrounding the peak inflow, similar to normal heart. At end diastole, a large rotating flow occupies the dilated ventricle. Flow along the septum turns back toward the mid ventricle rather than being directed toward the aortic valve (white arrow). In mid systole, the recirculation in the ventricular cavity persists even during ejection. LA indicates left atrium; A, ascending aorta.
A surprising feature of the LV, as viewed with flow-based methods, is its functional interior size. The endocardium is the internal limit of the chamber when flow is ignored, but in the full and beating heart, the functional limit to the interior of the ventricle may be different. The diastolic inflow does not enter an empty ventricle; there is blood in the LV at the end of systole that will be repositioned as the new blood rushes in. The residual volume of the LV (the portion of the LV volume that is inside the heart at the onset of diastole and is not ejected during the next systole) determines how much intracardiac volume is available for the exchanging components of the blood volume. The residual volume occupies a part of the LV that is less used by the exchanging blood flow. In this way, it outlines the functional periphery of the chamber and provides a fluid-fluid interface that influences the routes of the exchanging blood flow. The coarser trabeculations of more apical walls might augment deceleration of the exchanging blood, but the “padding” of those regions by the residual volume may allow smoother turning and preservation of the kinetic energy of the moving inflow. The limits, dynamic size, and shape of the LV functional interior defined in this way and visualized with 4D approaches are distinct from the limits demonstrated using pathlines representing the entire LV end-diastolic volume. Direct diastolic inflow (red) enters and exits the LV in a single heart beat. Retained inflow (yellow) enters but does not exit the LV in the same heart beat. Delayed ejection volume (green) begins diastole already in the LV and exits during systole. Residual volume (blue) begins and ends the cardiac cycle in the LV. Components are shown in early diastole (left), with atrial contraction (middle), and at mid systole (right). In the normal heart, the residual volume and delayed ejection volume are clearly seen lining the periphery of the apical chamber (left); there is extension of the inflow beyond the mid ventricle toward the apex in diastole (middle). In the failing heart, the increased residual volume occupies the apical LV (left); the extension of the inflow into the LV is limited to the basal regions (middle). The timing curve reflects the local velocities at the mitral (red) and aortic (green) valves. LA indicates left atrium; A, ascending aorta.
conventional assumptions. It is easy to anticipate that the failing heart should be associated with an alteration of this functional interior and the flow components passing through it.

**The Failing Heart: Passing Strange**

The increased end-systolic volume of a dilated, hypocontractile ventricle predicts an increased residual volume. Four-dimensional flow data demonstrate the extent and location of this volume and emphasize its low velocities, lack of exchange, and impact on the size of the functional interior of the ventricle. The exchanging components of diastolic flow in these enlarged hearts are paradoxically constrained to a smaller space than we would expect from conventional imaging tools.

The other flow components within the failing LV are also abnormal (Figure 2; supplemental Video III). The LV flow as visualized in the long axis plane is altered at all stages of the cardiac cycle (Figure 1; supplemental Video IV). Changes that are readily apparent on gross inspection include the size, position, and persistence of vortical flow structures. In contrast to normal ventricles, abnormal hearts show a larger mass of recirculating flow within the chamber, where rotating momentum results in persistence of velocities oriented away from the left ventricular outflow tract during isovolumic contraction and early systole. Normal ventricles demonstrate vortices limited to the basal chamber during diastole that rapidly unravel and extinguish during the earliest phases of ejection. Furthermore, in the normal heart at end diastole, the ejection volume is already moving toward the aortic valve and only needs to be accelerated in the direction in which the blood is already moving. In the failing heart, in contrast, the portion of the stroke volume that is entrained in the rotating volume and moving in the direction opposite to outflow must be both reaccelerated and redirected. Quantitatively, the differences between normal and failing ventricles become more apparent when the preservation of the kinetic energy of the inflow volume is considered.

The proportion of the total diastolic inflow that transits directly through the LV seems to vary with the acuity of the disease, but in all cases, it is less than in normal hearts, irrespective of clinical compensation. The shift in the relative proportions of direct and retained inflow in heart failure comes at a measurable cost in conservation of kinetic energy because the retained inflow loses more kinetic energy per milliliter than the direct flow. This reflects the deceleration of the blood components that do not achieve ejection; they must slow and be repositioned in the LV to await eventual reacceleration for ejection during a subsequent beat. That reacceleration may be accomplished in part by the momentum contributed by the next phase of fresh inflow from the subsequent diastole, combined with myocardial contraction, elevation of LV pressure and motion of walls and atrioventricular annulus.

It is encouraging to note that in patients with heart failure who are well compensated, the flow pattern within the LV seems less disordered than what we have observed in a patient who is less well-compensated (Table). However, despite the compensated clinical state, failing hearts seem to exhibit an increase in residual volume and impaired preservation of the kinetic energy of the diastolic inflow compared with normal hearts. Whether the optimization of the flow distribution and energetics will be a marker of good therapeutic response remains to be proven. An improvement in the amount and exchange of residual volume, vortical extent and rotation, and reduction of kinetic energy loss of the diastolic inflow are possible candidates for indicators of compensation of a dysfunctional heart. Defining the utility of these new, previously unobtainable measures of ventricular function will be the next step in applying these flow-based measures.

The flow patterns of the failing heart with preserved ejection fraction, diastolic dysfunction, or regional wall motion abnormalities will need to be carefully contrasted with the hypocontractile state. Preliminary studies have suggested distorted intracavitary blood flow patterns in hypertrophied hearts, with exaggeration of the submitral vortices and less penetration of new inflow to the apex. A region of segmental hypokinesis may be overlain by a volume of recirculating flow. This can be seen to distort the routes of other flow components. The patient’s specific combination of flow distortions may be a useful key to individualizing therapies if the optimization of flow distribution is shown to be predictive or impactful.

Beyond flow components and kinetic energy losses, multidimensional flow measurements can provide other novel measures of cardiovascular blood flow. One important advance under investigation addresses the long-standing problem of in vivo quantification and visualization of turbulence intensity (Figure 4). By exploiting the effects of flow velocity fluctuations on the measured MRI signal, the extent, the degree, and the timing of turbulence intensity at sites of aortic coarctation, valvular insufficiency, and post-mitral valve repair can be estimated. It is also possible to move from the phase-contrast data to dynamic regional maps of the relative pressure within the cardiac chambers, and these may correlate with specific abnormalities of ventricular function.

The approaches that have been discussed here for the LV also can be applied to the studies of the blood flow in other cardiac and vascular chambers. The left atrial blood has well-organized vortical flow structures that arise and extinguish in both systole and diastole and help to define the routes of the flow from pulmonary veins to the mitral annulus. The extent to which this flow arrangement is distorted by changes in atrial confines, rhythm, or ventricular abnormalities is an interesting topic for future investigation. Flow in the right

---

**Table. Trends in Relative Volume of Ventricular Flow Components**

<table>
<thead>
<tr>
<th>Flow Components</th>
<th>Normal</th>
<th>Mild CHF</th>
<th>Moderate CHF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inflow volume</td>
<td>Direct&gt;=retained</td>
<td>Direct=retained</td>
<td>Direct=&lt;retained</td>
</tr>
<tr>
<td>Loss of kinetic energy per mL inflow</td>
<td>Direct=&lt;retained</td>
<td>Direct=retained</td>
<td>Direct=&lt;retained</td>
</tr>
<tr>
<td>Residual volume/total LV end-diastolic volume</td>
<td>&lt;30%</td>
<td>&gt;30%</td>
<td>&gt;50%</td>
</tr>
</tbody>
</table>

CHF indicates congestive heart failure.
Matching Therapy to Flow

Flow-based measurements of ventricular function have yet to be investigated across the spectrum of cardiac diseases. It can be speculated that the interactions and energetic behavior of flow components in the cardiac chambers may provide a method for assessing heart failure therapies.32–37 In a failing ventricle, for example, a specific range of heart rates at which atrial contraction optimally contributes to presystolic events might be associated with improved proportion of direct flow and kinetic energy preservation. Alternatively, the amount and behavior of the residual volume might be predictive of thrombotic risk and be helpful in decisions regarding anticoagulation.

Dyscoordinate filling and contraction may contribute to the abnormal and inefficient flow characteristics demonstrated in patients with heart failure. Specific abnormal ventricular flow behaviors might prove useful in predicting response to cardiac resynchronization.38,39 More effective interactions between flow components might be restored if well-calibrated resynchronization is provided, and whether flow patterns would improve individual optimization of settings could be investigated. This work will be greatly facilitated as MRI-safe devices become available.

Prosthetic valve designs generally have been based on assumed flow fields extrapolated from normal hearts. Because these devices are intended for implantation in abnormal hearts with individual combinations of anatomic and flow distortions, it is interesting to consider how knowledge of abnormal flow in diseased hearts might improve prosthetic design and allow individualization of prosthetic selection and surgical approach. Ventricular remodeling procedures also are being investigated with multidimensional flow analysis to determine the changes in flow organization and efficiency that can be observed in the resized and reconfigured ventricle.

Summary

Multidimensional flow-based investigations of failing hearts may allow us to fill long-standing gaps in our knowledge about cardiovascular blood flow. The dynamic 4D images can provide an intuitive perspective on the flow, but their quantification will be required to clarify and compare health and diseases. Numeric estimates of measures of flow volumes, kinetic energy losses, or other features may eventually provide useful parameters for predicting and measuring response to therapy such as biventricular pacing, surgical approaches, and hemodynamic modifications. Understanding the normal mechanisms of flow apportionment and preservation of kinetic energy may allow us to define impairment in cardiac function in novel ways that are complementary to parameters based on wall motion and chamber dimensions. The early hypothesis that the volume flowing directly through the LV will preserve more of its initial kinetic energy and that the relative volume and energy changes of direct flow are markers of overall ventricular efficiency is under investigation across the spectrum of diseases. These nascent approaches to flow separation and quantification of kinetic energy losses hopefully will stimulate other novel investigations, leading to better design and matching of devices, therapies, and pacing to individual patients with heart failure.

Sources of Funding

This work was funded in part by the Swedish Research Council and the Swedish Heart and Lung Foundation. Dr Carlhall received funding from the Emil and Wera Cornell Foundation.

Disclosures

None.

References


