Intraventricular Flow During Isovolumic Relaxation: Description and Characterization by Doppler Echocardiography

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This study describes the characteristics of a prominent Doppler flow velocity signal representing intraventricular flow during left ventricular isovolumic relaxation. The flow during the isovolumic relaxation period was demonstrated in 60 subjects, including 7 with a normal heart, 26 with hypertrophic cardiomyopathy, 10 with aortic valve disease, 9 with a transplanted heart and 8 others. All had normal to hyperdynamic left ventricular systolic function with some degree of cavity obliteration as seen in the apical two-dimensional echocardiographic views. In contrast, this isovolumic relaxation period flow could not be demonstrated in the absence of cavity obliteration in any of 20 patients with either normal or diminished left ventricular systolic function.

Isovolumic relaxation period flow was best recorded from the apical transducer position and was directed toward the apex in all patients. By pulsed wave, and with two-dimensional Doppler ultrasound, the isovolumic relaxation period flow originated within a narrow area in the medial portion of the left ventricle along the middle or basal segments of the interventricular septum, but was recorded over a larger area toward the apex. The peak isovolumic relaxation period flow velocity was recorded just basal to the area of cavity obliteration, usually at the level of the papillary muscles, and ranged from 0.4 to 2.3 m/s (mean of 1.0 m/s). This isovolumic relaxation period flow started with aortic valve closure and, in 50 of the 60 patients, it lasted throughout isovolumic relaxation until mitral valve opening. In the other 10 patients (all with hypertrophic cardiomyopathy), it lasted for only a part (mean 63%) of this period. Because of its timing and appearance, this isovolumic relaxation period flow potentially could be confused with the early peak of the diastolic transmitral Doppler flow velocity signal.

(Doppler echocardiography has facilitated understanding of intracardiac blood flow by allowing for accurate evaluation of the presence, location, velocity and timing of various intracardiac blood flow patterns (1). The present study was prompted by a striking Doppler signal demonstrating an apically directed high blood flow velocity during the left ventricular isovolumic relaxation period in a patient with hypertrophic cardiomyopathy and cavity obliteration (Fig. 1, right panel). The presence and timing of this apparent intraventricular flow was recognized with continuous wave Doppler ultrasound, and its precise location within the left ventricle was determined with the pulse wave technique. We have subsequently documented a similar flow pattern in many other patients, with and without organic heart disease. The description of this flow pattern, the associated echocardiographic findings in the different patient groups and its relation to left ventricular cineangiographic studies form the basis of this report.

Methods

Study patients. The study group consisted of the first 60 patients undergoing a combined two-dimensional and Doppler echocardiogram at the Stanford echocardiography laboratory who were demonstrated to have a distinct flow velocity signal during left ventricular isovolumic relaxation. During this collection period approximately 1,200 patients were studied in the laboratory. The patients were referred to the echocardiography laboratory for routine cardiac assessment or were studied as part of other ongoing clinical research protocols. There were 40 men and 20 women; mean age was 54.2 years (range 17 to 80). Their cardiac diagnoses are listed in Table 1.

In addition, the two-dimensional echocardiographic char-
patients with coronary artery disease and at least one previous myocardial infarction, three patients with left ventricular hypertrophy presenting with congestive heart failure (one with hypertrophic cardiomyopathy and two with critical aortic stenosis), one patient with mitral valve prolapse and five patients with a normal heart.

**Two-dimensional and Doppler echocardiographic studies.** We used commercially available ultrasound equipment with continuous wave and pulsed wave capabilities (Hewlett Packard 77020, Irex Exemplar 3B, Irex Meridian, and VingMed SD-100). The two-dimensional and Doppler studies were performed with the patients in the supine or left lateral decubitus position. Multiple transducer positions including the apex and suprasternal notch were used. All patients were studied at rest. The two-dimensional images were obtained using the 2.5 or 3.5 MHz transducers.

**Continuous wave Doppler studies** were done using either or both a nonimaging 2.0 MHz transducer and an imaging transducer with continuous wave capability. Pulsed wave Doppler study was performed with an imaging transducer. A low pulse repetition frequency was used during the pulsed wave study; however, when the flow velocities exceeded the Nyquist limit a high pulse repetition frequency mode was used as well. Careful attention was paid to placing the additional sample volumes at sites outside the heart or at intracardiac sites where the pattern of flow was known, to avoid potential confusion of signals from the other sample volumes. In both the continuous wave and pulsed wave ultrasound studies the wall motion filter was usually kept at a low setting (300 Hz) to optimize the Doppler spectral display of the low velocity signals. A higher setting (600 Hz) was used to best display high velocity signals.

**Using the aortic and mitral valve opening and closure signals** (as recorded by Doppler echocardiography) in con-
junction with the simultaneously recorded electrocardiogram (ECG), the flow patterns recorded could be assigned to these phases of the cardiac cycle: left ventricular ejection, left ventricular filling and isovolumetric period. Isovolumic relaxation was defined as the interval between aortic valve closure and mitral valve opening. Valve motion appeared as sharp, well defined high intensity signals of short duration on the Doppler spectral display (Fig. 1, left panel). For the purpose of this report, we termed the flow occurring during isovolumic relaxation as isovolumic relaxation flow. When describing the diastolic mitral inflow signal, the early peak velocity of rapid ventricular filling is termed the E point, and the late peak velocity of atrial contraction is referred to as the A point. The ratio of peak isovolumic relaxation flow velocity to the E point velocity was calculated.

A two-dimensional Doppler flow velocity (color flow mapping) study was also performed using the Johnson & Johnson Aloka 880 instrument when available (20 patients). For precise timing the two-dimensional Doppler flow signal obtained from a single ultrasound beam path (M-mode) was displayed simultaneously with a pulsed wave signal obtained with the sample volume placed at a site along that same path. The standard Doppler display format was used, with flow toward the transducer displayed above the baseline, and flow away from the transducer below the baseline.

Cineangiography. Left ventricular cineangiograms of 13 patients (seven after heart transplantation and six with hypertrophic cardiomyopathy) undergoing Doppler and angiographic studies within 24 hours of each other were carefully reviewed for ventricular shape changes occurring during the isovolumic relaxation period. The patients were studied at rest; no changes in cardiac medications were made between the two studies. The cineangiograms were filmed at 60 frames/s. Ectopic and postectopic beats were not analyzed.

Isovolumic relaxation was defined as the period between the minimal ventricular area and mitral valve opening as identified angiographically (2,3). Successive frames from end-systole to mitral valve opening then were traced and analyzed. Ventricular shape change was defined as progressive outward motion of left ventricular wall segments, seen when cavity outlines of successive frames were superimposed.

Results

Two-dimensional echocardiographic characteristics. On the basis of echocardiographic evaluation, all 60 patients with isovolumic relaxation flow had either normal or hyperdynamic left ventricular contraction associated with some degree of cavity obliteration in the standard two-dimensional apical views. Cavity obliteration was seen in the apical four chamber view alone or in the apical two chamber view additionally. The questions of whether the left ventricular cavity was completely obliterated, whether a small volume of blood remained trapped in lacunae created by trabeculae within the left ventricle or whether there was separation of the cavity into a tiny apical chamber and a larger basal chamber were beyond the resolution of the two-dimensional images.

In contrast, the 20 patients without recorded isovolumic relaxation flow had either normal or poor left ventricular systolic function, and none demonstrated cavity obliteration. The four patients with coronary artery disease had sustained a previous myocardial infarction, and three had a left ventricular aneurysm.

Doppler flow characteristics. The following points will serve to illustrate and characterize the Doppler flow velocity signal seen during isovolumic relaxation.

1. Although multiple transducer sites were attempted, the isovolumic relaxation flow signal was always best obtained from the apical transducer position. The flow was directed toward the apex in all 60 patients.

2. Using continuous wave Doppler ultrasound, the signal was encountered by directing the beam from the left ventricular apex toward the mitral valve or toward the left ventricular outflow tract and aortic valve. The flow velocity varied with the path of the beam within the left ventricular cavity. The highest velocity signal was obtained with the beam traversing the area of cavity obliteration.

3. With pulsed wave Doppler ultrasound, the highest velocity isovolumic relaxation flow signal was in close prox-
iminity to the cavity obliteration. This was just basal to the area of cavity obliteration in the medial part of the left ventricle as seen in the two-dimensional apical four chamber view. This site varied from patient to patient, and was closer to the apex in patients with lesser degrees of cavity obliteration, and further from the apex in those with marked cavity obliteration. In general it was at the level of the papillary muscle heads, seen in the apical four chamber view, as they contracted in systole.

4. The size and location of this signal in the left ventricle was ascertained by careful pulsed wave mapping in the apical four chamber view. It originated within a narrow area in the medial portion of the left ventricle adjacent to the interventricular septum. The site of origin in most patients was along the middle one-third of the septum; however, this was variable and in one patient the flow originated just below the aortic valve. The flow could then be traced from the point of origin toward the apex along the interventricular septum. Although the area of flow at the origin was narrow and located adjacent to the septum, it was of variable width toward the apex and was found near the free wall of the left ventricle in some cases.

5. The flow signal during isovolumic relaxation was distinct and separate from the mitral inflow signal. The continuous wave spectral recordings toward the mitral valve orifice (in the 58 patients with normal sinus rhythm) displayed a characteristic “triple peaked” signal. Careful attention to the aortic and mitral valve clicks demonstrated the first peak to correspond to flow during isovolumic relaxation (between aortic valve closure and mitral valve opening). The latter two peaks of the signal started with mitral valve opening and corresponded to the E and A points of the mitral flow signal (Fig. 1). Furthermore, in six of our patients with concomitant mitral regurgitation, continuous wave Doppler study displayed the isovolumic relaxation flow and mitral regurgitation signals as two distinct but simultaneously occurring flow signals with opposite directions and terminating with mitral valve opening (Fig. 2). This suggests that the two signals originate at different sites within the path of the beam, and provides further evidence that the isovolumic relaxation flow signal is separate and
Figure 4. Pulsed wave Doppler flow velocity tracing in a patient with hypertrophic cardiomyopathy, obtained from the apical position with the sample volume within the left ventricular cavity at the level of the papillary muscles. Forward systolic flow below the baseline is late peaking and is continuous with (small arrows) the apically directed isovolumic relaxation flow (IVRF) above the baseline. In this case the apically directed isovolumic relaxation flow lasts for only a portion of the isovolumic relaxation period. During the latter part of this period a separate signal (open arrows) appears, directed away from the apex and lasting until mitral valve opening (MVO). Calibration dots = 0.5 m/s.

distinct from the mitral flow signal. These two signals could be separated using pulsed wave Doppler ultrasound as well. The isovolumic relaxation flow signal was never found at the mitral orifice but, as mentioned, was tracked near the interventricular septum. Although in some patients with a small ventricle the two signals were in close proximity, the true mitral inflow signal could be obtained by placing the sample volume at, or just on the atrial side of, the mitral valve orifice (Fig. 3).

6. Peak velocity of the isovolumic relaxation flow ranged from 0.4 to 2.3 m/s (mean 1.0). The ratio of peak isovolumic relaxation flow velocity to the E point velocity also varied widely among patients, and ranged from <1:1 to >2:1.

7. In the majority of cases (50 of 60 patients) the isovolumic relaxation flow lasted throughout the isovolumic relaxation period. However, in 10 patients (all with hypertrophic cardiomyopathy) this flow lasted for only a portion (mean 63%, range 30 to 83%) of that period. Nine of

Figure 5. Two-dimensional Doppler flow velocity color mapping from the apical transducer position in a patient with isovolumic relaxation flow. A, Stop-frame during isovolumic relaxation demonstrating a prominent, apically directed (red) flow velocity signal. It originates in a narrow area within the left ventricular (LV) outflow tract just below the aortic (A.) valve, and spreads in area toward the apex. B, The next frame (after A) in the same cardiac cycle, demonstrating early diastolic left ventricular filling through the open mitral valve. C, Pulsed wave Doppler spectral display (lower panel) at the level of the papillary muscles with simultaneous two-dimensional Doppler M-mode tracing (upper panel) along the same beam path. The apically directed, red isovolumic relaxation flow (IVRF) signal seen in the upper panel corresponds in time and location to that on the pulsed wave tracing in the lower panel, and is followed by the E and A peaks of the diastolic transmitral flow. LA = left atrium; LV = left ventricle.
Figure 6. Right anterior oblique cineangiographic stop-frames during one cardiac cycle in a patient with hypertrophic cardiomyopathy demonstrated to have isovolumic relaxation flow by Doppler study. A, End-diastole; B, end-systole; and C, stop frame during isovolumic relaxation, before mitral valve opening, showing outward motion of the apex (small arrows) as compared with end-systole.

these 10 patients demonstrated a flow signal in the opposite direction (away from the apex) in the latter part of isovolumic relaxation and continuing until mitral valve opening (Fig. 4).

8. Continuous wave Doppler ultrasound in patients with a hypertrophied or hyperdynamic ventricle having concomitant cavity obliteration often demonstrates a mid to late systolic rise in forward flow velocity, which can be shown by pulsed wave Doppler ultrasound, to originate in the area of cavity obliteration. This is distinct from the Doppler signal obtained across the left ventricular outflow tract in patients with hypertrophic cardiomyopathy with an outflow tract gradient (4). Of the 36 patients with echocardiographic left ventricular hypertrophy in our group, this systolic flow velocity signal from the apex was present in 34 (94%) with a mean peak velocity of 1.3 m/s (range 0.5 to 4.0) (Fig. 4). It was also present in 11 of 15 patients without left ventricular hypertrophy (mean 0.7, range 0.3 to 1.6 m/s) but in none of the nine patients with a transplanted heart.

We carefully assessed the precise site and timing of that systolic apical flow in relation to isovolumic relaxation flow in 10 of our patients using pulsed wave Doppler ultrasound. In each patient, both flow signals (mid to late systolic flow away from the apex and isovolumic relaxation flow toward the apex) were recorded at the same volume site, just basal to the area of cavity obliteration. Furthermore, the end of the forward flow signal was continuous with the onset of the reversal during the isovolumic relaxation flow signal (Fig. 4).

9. Two-dimensional Doppler flow velocity color mapping was used in 20 of our patients. In these, frame by frame analysis showed an apically directed (red colored) flow velocity jet of short duration (Fig. 5). It appeared after aortic closure and disappeared by the time of mitral valve opening.

It originated within the medial portion of the left ventricle near the interventricular septum, but the length, width and site along the interventricular septum varied from patient to patient. It could be distinguished from initial mitral inflow both by its timing (before mitral valve opening) and by its location. Exact timing was also assessed with simultaneous pulsed wave Doppler ultrasound (displaying the isovolumic relaxation flow) and M-mode display of the two-dimensional flow velocity signal obtained at that beam direction (Fig. 5). This confirmed the timing of the two-dimensional Doppler signal just described and showed it to correspond precisely to the isovolumic relaxation flow signal obtained with regular pulsed wave Doppler ultrasound.

Cineangiographic characteristics. Each of the 13 cineangiograms analyzed showed definite left ventricular
shape changes during isovolumic relaxation (Fig. 6). These
shape changes were outward motion of the anterior or apical
left ventricular wall segments, or both, as seen in the right
anterior oblique ventriculogram. None of these 13 patients
had clinical or Doppler evidence of aortic regurgitation. In
nine patients the segmental outward motion progressed
throughout the isovolumic relaxation period and was max­
imal at mitral valve opening. In the remaining four patients
(all with hypertrophic cardiomyopathy), segmental outward
motion reached a maximum part way through the isovolumic
relaxation period. During the latter part of isovolumic re­
 laxation the segments involved recoiled back with an inward
motion that progressed until mitral valve opening.

Discussion

Association with left ventricular function. A distinct
intraventricular flow pattern occurring during isovolumic
relaxation has been observed and characterized with con­
tinuous wave, pulsed wave and two-dimensional Doppler
flow velocity mapping. All 60 patients with this signal had
at least normal left ventricular systolic function and all had
some degree of cavity obliteration as seen in the standard
two-dimensional apical views. In contrast, it could not be
demonstrated in any of the 20 patients with either normal
or poor left ventricular systolic function but without cavity
obliteration. Although the distribution of cardiac diseases
differs between the groups with and without intraventricular
flow signals during isovolumic relaxation, there seems to
be an association between the finding of normal or hyper­
dynamic systolic function with cavity obliteration and the
presence of a well defined intraventricular flow signal to­tward the obliterated cavity during isovolumic relaxation.

Potential pitfalls. A potentially important point regard­
ing this flow velocity signal is that with continuous wave
Doppler recording, it may be confused with the E point of
the mitral signal and thus become a source of erroneous
mitral pressure half-time measurements or interpretation of
atrioventricular (AV) pressure differences when assessing
ventricular diastolic function. Awareness of this pitfall may
lead to its recognition in patients with sinus rhythm when
three diastolic flow velocity peaks are not noted. In patients
with atrial fibrillation, a double peaked signal due to iso­
volumic relaxation flow followed by the mitral E point is
seen (Fig. 7). Careful attention to timing of the aortic and
mitral valve clicks on Doppler records shows this flow to
occur between aortic valve closure and mitral valve opening.
In patients with mitral regurgitation this flow occurs during
the terminal period of mitral regurgitation but usually has
an opposite direction. By switching to the pulsed wave mode
and placing the sample volume at the mitral orifice, iso­
volumic relaxation flow is not recorded and the true mitral
inflow signal is obtained.

With two-dimensional Doppler flow velocity color map­
ing the isovolumic relaxation flow signal might be confused
with aortic regurgitation. Both may appear as apically di­
rected flow velocities originating in the left ventricular out­
flow tract, and both start after aortic valve closure (Fig. 5).
However, isovolumic relaxation flow is usually of low ve­
locity with minimal turbulence appearing as a homogeneous
red color whereas aortic regurgitant flow is of high velocity
and turbulence, appearing as a mosaic of red-yellow and
blue-green colors on two-dimensional Doppler echocardi­
gram.

Underlying mechanisms. Left ventricular shape changes
during isovolumic relaxation, seen as outward motion of
left ventricular wall segments, has been previously de­
scribed by cineangiography. The segments involved were
usually the anterior and apical segments. This phenomenon
has been variously termed systolic early relaxation phenom­
enon, preinfow relaxation, late systolic bulging and asyn­
chronous segmental relaxation (2,3,5–8). In the present study,
ventricular shape changes involving the anterior or apical
segments, or both, occurred during isovolumic relaxation
in each of the 13 cineangiograms reviewed. The isovolumic
relaxation flow described in this study is consistent with the
intraventricular redistribution of blood that must accompany
these shape changes.

The precise cause or underlying mechanism responsible
for this described flow is unclear. However, because this
flow is 1) associated with good left ventricular systolic func­
tion and cavity obliteration, 2) directed toward the site of
cavity obliteration, and 3) associated with isovolumic out­
ward motion of the left ventricular wall segments, it is likely
due to intraventricular pressure differences created by asyn­
chronous early relaxation of the wall segments surrounding
the obliterated cavity (9). Minor degrees of asynchronous
relaxation may well be a normal phenomenon, becoming
more pronounced in hyperdynamic states. Additionally or
alternatively, in at least some patients with left ventricular
hypertrophy and cavity obliteration, a mid to late systolic
forward flow signal of higher velocity than otherwise ex­
pected from the apex often appears, originating within and
dissipating a short distance beyond the obliterated cavity
(4). It is a prominent signal with a rapidly accelerating flow
velocity that abruptly terminates in late systole. It may be
generated by blood being ejected from the apex into the
body of the left ventricle presumably because of intraven­
tricular pressure differences created as the wall segments
surrounding the apical portion of the left ventricle squeeze
and obliterate the apical cavity. This late systolic increase
in pressure may serve as a late systolic relaxation load,
acting to enhance the rate of relaxation of the wall segments
involved (10). This is supported in 10 of our patients in
whom late systolic and isovolumic relaxation flows were
present at the same location, just basal to the site of cavity
obliteration, and were virtually continuous with each other
at that location (Fig. 4). Thus, it is likely that the segments
involved in the generation of the late systolic flow signal are the same segments involved in the generation of the isovolumic relaxation flow. This hypothesis may explain our findings in a particular subgroup of patients with left ventricular hypertrophy, specifically those in whom the late systolic flow velocity represents a sufficient increase in intraventricular pressure difference so as to act as a relaxation load.

Finally, although the isovolumic relaxation flow signal may be very prominent in its intensity and velocity, the actual volume of blood associated with it is not quantifiable. In the majority of cases it is likely very small, although based on a previous cineangiographic study with volume analysis, it may be as much as 22% of the stroke volume (2).

References