Regional Stasis of Blood in the Dysfunctional Left Ventricle: Echocardiographic Detection and Differentiation from Early Thrombosis

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SUMMARY In two-dimensional echocardiographic studies of left ventricular thrombus in patients, an unusual pattern of dynamic left ventricular intracavitary echoes was identified in some hearts with severe apical dysfunction. These intracavitary echoes were noted in the apical region and were distinct from left ventricular thrombi. Certain features of the intracavitary echoes suggested that they were generated by regional stasis of blood. To study this phenomenon, echocardiography was performed in 11 dogs with experimental anteroseptal infarction and associated left ventricular thrombus and in six dogs with infarction but no thrombus. The dynamic intracavitary echo pattern suggesting blood stasis was identified in the ischemic apex in dogs of both groups. These echoes had characteristics suggesting a fluid or semifluid state and could be distinguished from thrombi. In real time, the echoes moved in a slow, circular fashion at the apex and lacked well-defined borders; their configuration and acoustic intensity changed over short periods of time, and they could be rapidly altered by ectopic or mechanical contraction of the heart and by dopamine infusion. Postmortem examination showed that liquid blood produced the echoes.

Additional studies demonstrated the echogenicity of static blood. Echocardiography of dog hearts with KCl-induced mechanical asystole showed the rapid development of diffuse echogenicity of the intraventricular contents; in vitro studies confirmed the echogenicity of static blood.

These observations indicate that a spectrum of echocardiographic features characterizes ventricular blood under various conditions of flow and with frank thrombosis. The ability of echocardiography to detect in vivo stasis of blood in the left ventricle and to distinguish this from thrombosis has important clinical and investigational implications.

IN 1975, using M-mode echocardiography, Feigenbaum described accumulations of intracavitary echoes next to dysskinetic segments of the left ventricular wall in patients with coronary artery disease. He thought these echoes were generated by sluggish blood flow in the area of regional ventricular dysfunction. More recently, Sigel et al. demonstrated the echogenicity of static blood in both in vitro experiments and in the totally occluded canine vena cava. In studies of left ventricular thrombus using two-dimensional echocardiography, we noted dynamic intracavitary echoes in the apex of some patients with severe apical wall motion abnormalities; these echoes were distinct from thrombus and had characteristics suggesting that their source was blood stasis. In studies of experimental left ventricular thrombosis in dogs we also found that these dynamic-intracavitary echoes were distinct from thrombi.

In this report, we present the characteristics of these intracavitary echoes in man and in dogs and the results of animal studies.

Materials and Methods

Definitions

The following terms are defined as they are used in the manuscript:

Dynamic intracavitary echoes — the pattern of echoes in the ventricular apex that suggests regional stasis of blood.

Blood stasis — slowing of blood flow velocity from normal conditions.

Static blood — blood with complete cessation of flow.

Echodensity — a qualitative term describing the relative acoustic intensity of echoes produced by a substance, i.e., the greater the echodensity of an echo target the more intense and visible the echoes produced for a given ultrasonic gain and reject setting.

Patient Studies

We reviewed approximately 2800 consecutive two-dimensional echocardiograms performed over a 2½-year period. Forty-nine patients had echocardiograms either diagnostic or highly suggestive of left ventricular thrombus by previously reported criteria. The patients were studied with a mechanical sector scanner (Advanced Technologies Laboratory, Mark III) and a 3-MHz transducer. A systematic examination was performed in parasternal, apical and subcostal acoustic views with varying sector orientations. The apical precordial view was the most useful for detecting both thrombus and the echocardiographic patterns associated with blood stasis. For the apical views, patients were examined in the left lateral decubitus position.
with the head slightly elevated and the transducer placed at the point of maximal impulse. Shallow depth settings of 7 and 9 cm for the apical views were particularly helpful for detailed imaging and for maintaining good near-field resolution. In four patients in whom the echocardiographer suspected a pattern of dynamic intracavitary echoes on the routine examination, a 5-MHz transducer was applied to the apex with shallow depth settings to enhance near-field resolution. In three such patients, images were obtained with both the mechanical sector scanner and a phased-array ultrasonograph (Varian Instruments, Varian-3000), which has a 2.5-MHz transducer.

To obtain information on the incidence of the dynamic intracavitary echo pattern in patients with severe apical wall motion abnormalities, we reviewed 52 consecutive patients with electrocardiographic anterior myocardial infarction prospectively studied with two-dimensional echocardiography. These patients were originally studied to determine the incidence of left ventricular thrombosis in acute myocardial infarction. Myocardial infarction was defined by typical clinical history; evolutionary electrocardiographic changes, including the development of new Q waves; and typical serial cardiac enzyme patterns of total CK, the MB fraction of CK, and lactic dehydrogenase. No patient had historical or electrocardiographic evidence of prior myocardial infarction. Two-dimensional echocardiography was performed within 72 hours of admission and serially during hospitalization. In each patient, apical wall motion was analyzed and classified as normal, hypokinetic, akinetic or dyskinetic.

Experimental Animal Studies

Animal Preparation

Studies were performed in 17 mongrel dogs that weighed 17–30 kg. The dogs were anesthetized with i.v. pentobarbital, 20–25 mg/kg, supplemented as required, and ventilated with a positive-pressure respirator with supplemental oxygen. The heart rate was monitored by ECG. The heart was exposed through a midline sternotomy and suspended in a pericardial sling. Baseline two-dimensional echocardiograms were then obtained. After i.v. lidocaine, 2 mg/kg, was given, the middle portion of the left anterior descending coronary artery was ligated. Additional epicardial coronary arteries supplying the apex were identified and ligated near the apex. This method of ligation produces transmural infarction and generates an echocardiographic pattern of abnormal apical wall motion similar to that in patients with anterior myocardial infarction. The dogs were allowed to stabilize for 15–20 minutes and echocardiograms were obtained to document the wall motion abnormality induced by coronary ligation.

In 11 of the 17 dogs (group 1), left ventricular mural thrombi were generated by injecting several 0.25-ml volumes of 5% sodium ricinoleate into the apical subendocardium. Sodium ricinoleate is a free fatty acid ester that acts as a sclerosing agent to produce subendocardial injury and provide a nidus for thrombus formation. The dogs were allowed to stabilize, and serial echocardiographic images were obtained at 20–30-minute intervals over the next 4–8 hours. These 11 dogs were studied echocardiographically until a definite mural thrombus was detected and its size remained stable for 1–2 hours.

In the remaining six dogs (group 2), coronary ligation was performed as in group 1, but sodium ricinoleate was not injected. Solandt et al. reported that thrombus does not usually acutely develop in this situation. Ischemic wall motion abnormalities were documented echocardiographically in these dogs. They were then followed with the serial echocardiographic protocol used in group 1.

In Vivo Experimental Interventions and Studies of Static Ventricular Blood

Several interventions were performed in the group 2 dogs to assess their effect on the dynamic intracavitary echocardiographic patterns. In three dogs, dopamine was infused. Pulmonary arterial, aortic and left ventricular pressures were measured and cardiac output was determined in triplicate by the indocyanine green dye technique using a cardiac output computer (Model RLD, Lexington Instruments). Hemodynamic variables were measured with simultaneous echocardiographic images before and during i.v. dopamine administration. 7.5 µg/kg/min, after the coronary ligation.

In three dogs, 5–10-ml boluses of normal saline were injected into the left ventricle or left atrium to obtain echocardiographic contrast ventriculograms. Saline was injected before and after coronary ligation, and echocardiograms were obtained simultaneously. In addition, external manual compression of the in vivo hearts was also performed during echocardiography in several group 2 dogs for one or two contractions so the effects of this maneuver on the intracavitary echoes could be viewed. Each tape was also reviewed for the effects of spontaneous ventricular ectopic contractions on the echocardiographic patterns.

After the last in vivo echocardiographic imaging, dogs from both groups were injected in a peripheral vein or the descending aorta with a concentrated potassium chloride solution. Continuous two-dimensional echocardiographic imaging was then performed in the majority of dogs until mechanical asystole had been present for several minutes. Several of the asystolic hearts were externally manually compressed while echocardiographic imaging was continued. The hearts were then removed. The aorta was clamped and the base of the heart and pulmonary veins tightly grasped and pulled ventrally to ensure that the left ventricle was in a dependent position during dissection and that ventricular contents did not escape during removal of the heart. The left ventricles were opened for gross inspection and the liquid contents were strained through small-pore cloths. Thrombi were measured as previously described. The hearts and thrombi were then
fixed in formalin and areas of the thrombi were sectioned for histologic examination.

**Echocardiography**

Echocardiographic imaging in the dogs was performed with the mechanical sector scanner (Advanced Technologies Laboratory, Mark III). The transducer was placed lightly on the exposed surface of the heart; aquasonic gel was used as a conduction medium. Echocardiographic views were obtained that showed the entire left ventricle and the apex in particular. These views included an anteromedial position at the mid-heart level with the sector orientation in the long axis of the heart and the left ventricular apex using multiple sector orientations in both the long- and short-axis planes of the heart. Although no effort was made to precisely simulate views obtained in patients, these two echocardiographic windows produced images similar to those obtained in patients with the parasternal long-axis view and the apical two- and four-chamber and apical short-axis views, respectively. In nine dogs, images were obtained with 3-MHz and 5-MHz transducers for comparison. Only the 5-MHz transducer was used in the other dogs.

The echocardiographic studies were interpreted by three experienced echocardiographers. In the last 11 dogs including all six in group 2, the tapes were interpreted blindly by an examiner not present in the laboratory when the studies were performed. The echocardiograms were recorded on ½- or ¼-inch videotapes for subsequent review.

**In Vitro Studies**

In vitro water bath studies using the same two-dimensional mechanical sector scanner were performed to further investigate the genesis of the intracavitary echo patterns seen in vivo. Whole blood specimens (6–8 ml) from a dog and from a human volunteer were drawn in buffered EDTA solution. The specimens were transferred into flexible latex tubes, 0.6 cm in diameter, sealed at one end. The tubes were clamped and suspended in a water bath, which served as an ultrasonic conduction medium. Another tube that contained a similar volume of saline was used as a control. The tubes were imaged with the 5-MHz transducer over the range of gain and reject settings of the echocardiographic instrument.

Using the same approach, platelet-rich plasma, platelet-poor plasma and stimulated platelet aggregates from both species were imaged in a water bath at a temperature of 37° C. Platelet-rich plasma was prepared at room temperature by collecting blood in plastic tubes containing 3.8% sodium citrate and centrifuging at room temperature at 800–1000 rpm for 10 minutes. The plasma was then separated and introduced into the latex tube. Platelet-poor plasma was similarly obtained and centrifuged at 3000 rpm for 10 minutes. Platelet aggregates were generated in the latex tube by injecting 1 ml of adenosine diphosphate, 10 μg/ml (Sigma #A0127) into the sealed latex tubes containing human or canine platelet-rich plasma. Platelet aggregation was confirmed by visual inspection and by aggregometry (Bio-Data Corp., model PAP-3). Echocardiographic imaging was performed in each specimen with and without mechanical agitation of the latex tube over the range of gain and reject settings.

**Results**

**Echocardiographic Pattern of Blood Stasis in Patients**

Nine patients had definite evidence of dynamic intracavitary echoes suggesting blood stasis in the left ventricle (table 1). These echoes were seen only in the apical region and had features suggesting a fluid or semifluid state. The echoes were of variable amplitude and density and moved in slow circles in the apical region (fig. 1). All nine patients had severe apical wall motion abnormalities with either akinesia or dyskinesis of the ventricular apex. Eight of the nine had a history of anterio myocardial infarction: four were recent (within 3 weeks) and four were remote. One patient had congestive cardiomyopathy. Three patients had clinical congestive heart failure requiring therapy; two were taking systemic anticoagulants at the time of imaging. Seven of the nine had echocardiographic evidence of associated mural thrombus at the apex. The thrombi were distinct from the dynamic intracavitary echoes in each patient. In one patient without an associated mural thrombus, the effect of sublingual nitroglycerin on the intracavitary echoes was examined. After nitroglycerin, the intracavitary echoes changed configuration and seemed to coalesce within the central portion of the apex. Over several minutes this coalescence receded and the echo pattern returned to the baseline state. In two other patients with abdominal aortic aneurysms (table 1), a similar pattern of echoes was noted within the aneurysmal aortic segment. In both, the echoes of blood stasis were distinct from those of mural thrombi in the aneurysm.

Forty-one of the 52 consecutive patients (79%) who had had their first anterior myocardial infarction had apical akinesia or dyskinesis present on at least one echocardiogram. Two of these 41 patients (5%) had dynamic intracavitary echoes suggesting blood stasis. One of these also had a mural thrombus echocardiographically. The other patient did not have a mural thrombus; subsequent echocardiograms showed that the apical wall motion had improved and the dynamic intracavitary echoes were absent.

In the three patients in whom the left ventricle was studied with both the mechanical sector scanner and the phased-array ultrasonograph, the intracavitary echoes were seen with both instruments. The echoes were more distinct on echocardiograms obtained with the mechanical sector scanner.

**Animal Experiments**

**Left Ventricular Apical Wall Motion Abnormalities**

Coronary ligation resulted in echocardiographically distinct apical wall motion abnormalities; each dog had akinesis or dyskinesia during systole (table 2). The
TABLE 1. Patients with Echocardiographic Evidence of Blood Stasis

<table>
<thead>
<tr>
<th>Pt</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Clinical setting</th>
<th>Location of echoes</th>
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<td>Aortic aneurysm</td>
<td>Abdomen</td>
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Abbreviations: AMI = anterior myocardial infarction; CCM = congestive cardiomyopathy.

A consistent echocardiographic feature that indicative of regional dysfunction in these dogs was qualitatively similar to that in the majority of patients with isolated acute anterior infarction reported by Asinger et al. 4

Echocardiographic Features of Experimental Acute Thrombosis and Histopathologic Correlates

In all dogs in group 1, left ventricular mural thrombi attached to the apical endocardium were imaged echocardiographically (fig. 2). The echocardiographic and histologic features of the thrombi have been reported in detail. 5 The mural thrombi were located at the apex. At autopsy, they were 0.6 × 0.5 to 2.1 × 2.0 cm. The echocardiograms showed that these endocardial mural thrombi had no significant intracavitary motion. In six of the 11 dogs, we found a portion of thrombus that was distinct from the endocardial portion. This second portion of thrombus was a tail-shaped mass that was attached to the endocardial thrombus and extended into the left ventricle (fig. 2). The tails moved during the cardiac cycle and had well-defined, consistent borders echocardiographically. These thrombi were less acoustically intense than the endocardial thrombi, but had homogeneous acoustic density.

Autopsy examination confirmed the presence of thrombus in all 11 dogs. Histologically, the endocardial thrombi were characterized by typical platelet lamellae bordered by leukocytes (lines of Zahn) interspersed among fragmented erythrocytes. In the dogs that had two distinct portions of thrombus echocardiographically, gross examination showed two distinct areas of thrombus. In these dogs, a tail-shaped red thrombus was attached to the endocardial thrombus and extended toward the outflow tract. The red tails differed from the endocardial thrombi and showed nonfragmented erythrocytes enmeshed in a fine fibrin network, with minimal or no platelet lamellae. 5

Both portions of the thrombi were seen by blinded observers reviewing the videotapes recorded during imaging with both the 3- and the 5-MHz transducer. The 5-MHz transducer, however, provided better near-field resolution and showed the less acoustically intense tail portions more clearly. The endocardial portions were of such acoustic intensity that no difference was noted between the transducers. 5

Intracavitary Echocardiographic Patterns of Regional Blood Stasis

In seven of the 11 dogs with left ventricular thrombi, an intracavitary pattern of echoes identical to that described above in patients was seen in the left ventricle (table 2). The ultrasonic pattern was characterized by low-amplitude, variable-density echoes that moved in slow circles within the dysfunctional apex. Echocardiographically, this pattern was distinct from both the endocardial and tail portions of thrombi. At postmortem examination, only liquid blood was found in the ventricle to explain the echoes.

In the six dogs that did not receive a ricinoleate injection, the intracavitary echo pattern was detected in the dysfunctional apex in the absence of echocardiographic evidence of mural thrombus (table 2, fig. 1C). As in patients (fig. 1A), the echoes in the dogs showed variable acoustic intensity and a slow, circular movement within the apical area. The most acoustically intense intracavitary echoes produced a pattern that simulated an endocardial thrombus if viewed for only one or two cardiac cycles (fig. 3A). The echoes occasionally formed a vortex that simulated the red thrombus tails seen in some group 1 dogs. Real-time images over several cardiac cycles, however, showed differences between this intracavitary echo pattern and that with thrombosis. In contrast to the echocardiographic picture of frank thrombosis, these intracavitary echo patterns lacked features suggesting a mass. The borders of the echoes were evanescent and poorly defined, and areas within the echoes appeared to coalesce and then disperse over several cardiac cycles. The intracavitary echoes had fluid characteristics and resembled smoke moving slowly through a light beam in a darkened room. In each group 2 dog, this echo pattern was seen within the ventricle in the absence of echocardiographic evidence of mural thrombus. At postmortem examination, only liquid blood that passed through the cloth filters was present in the ventricle.

A consistent echocardiographic feature that indicat-
ed the fluidity of these intracavitary echoes was their evanescent configuration and variable acoustic density, similar to that seen in the patient given nitroglycerin. Ventricular ectopic beats or external mechanical contraction of the heart immediately altered the shape and motion of the intracavitary echoes, as did infusion of dopamine. Figure 3 illustrates this phenomenon. This sequence of views was obtained during continuous imaging over several minutes without changing the transducer gain or reject settings. In figure 3A, a relatively dense group of echoes can be seen at the apex. The echoes have sufficient acoustic intensity and homogeneity to simulate a thrombus. A dopamine infusion was then initiated. Figure 3B, obtained a few cardiac cycles later after a short run of ventricular tachycardia, shows a rapid transformation in the configuration of the echoes into a large curl with the tip moving circularly. Figure 3C was obtained minutes later, after the hemodynamic effects of dopamine on heart rate and systolic blood pressure had occurred. The echoes have been completely dispersed from the central apical cavity, and in real time appeared to layer along the ventricular wall. After the dopamine infusion was stopped, the pre-dopamine pattern recurred. At autopsy shortly after this intervention, only liquid blood was found in the ventricle.

**Qualitative Patterns of Blood Flow in the Left Ventricle**

In three group 2 dogs, normal saline was injected into the left atrium or left ventricle before and after coronary ligation to generate an echocardiographic contrast medium. Before coronary ligation, the contrast echoes filled the ventricle uniformly and emptied

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**TABLE 2. Animal Studies**

<table>
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<tr>
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<th>Location</th>
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**Figure 1.** (A) Still-frame echocardiographic apical view in patient 7, who had a remote anterior myocardial infarction. Apical dyskinesis was seen in real-time images. The apical region contains low-amplitude, variable-density intracavitary echoes (arrow) that moved in a slow circle in the direction of the arrow. (B) Schematic of the fluid intracavitary echoes in figure 1A. (C) An echocardiogram from a dog in group 2. As in patients, the apex showed dyskinetic bulging, and dynamic intracavitary echoes were present (arrow). At autopsy, only liquid blood was present in the ventricle. LV = left ventricle; LA = left atrium.
within a few cardiac cycles. No regional accumulation of the contrast echoes was noted. After coronary ligation, contrast echoes entered the dysfunctional apical area and persisted, while echoes in the basilar portion of the ventricle cleared. The contrast echoes remained in the apical area moved in a circle, as did the intracavitary echoes (fig. 1). However, the echoes generated by saline injection had acoustic properties different from those of the intracavitary echoes.

**Studies on the Echogenicity of Static Blood**

Figure 4, obtained from a dog in group 1, illustrates an echocardiographic phenomenon seen after KCl injection. Before KCl injection, the echocardiograms showed an endocardial thrombus and dynamic intracavitary echoes at the apex (fig. 4A). As the blood pressure deteriorated after injection of KCl, but before complete mechanical asystole, the intracavitary echoes at the apex became more intense and homogenous. Similar low-density echoes began to develop in the

**Figure 2.** (A) Two-dimensional echocardiographic still frame from a dog in group 2 showing a left ventricular thrombus with two distinct portions. The endocardial mural thrombus (T) is attached to the apex and is acoustically dense. Attached to this is a large tail of thrombus (arrows) that is less acoustically intense and extends into the left ventricle. In real-time images, both components had well-defined borders and appeared as distinct masses. LV = left ventricle; Ao = aorta; LA = left atrium. (B) Schematic of figure 2A.

**Figure 3.** (A) Echocardiographic apical view from a dog in group 2 without associated thrombus. There is an extremely echo-dense pattern of blood stasis (arrows) at the apex. The acoustic density and shape of the echoes simulate a thrombus, but in real time, the entire mass of echoes moved circularly in the apical region. (B) The mass of echoes seen in figure 3A were rapidly transformed after a three-beat salvo of ventricular tachycardia as dopamine infusion was initiated. This instantly altered the acoustic density and the configuration of the echoes, and a curled pattern was produced (arrow). This view was obtained with the same transducer position and gain-reject settings used to obtain figure 3A, although the depth scale is reduced. (C) With the onset of a hemodynamic effect from dopamine, the apical echoes seen in figures 3A and 3B are now completely dispersed from the central portion of the apex. In real time, the echoes appeared to layer along the septal wall (arrows). After the dopamine infusion was stopped, the pattern shown in figure 3A recurred. Only liquid blood was found in the ventricle at autopsy.
Addition of adenosine diphosphate to plate-
let-rich plasma from both species produced grossly visible platelet aggregates, confirmed by aggregometry. Echocardiographic imaging showed no acoustic reflectiveness from the platelet aggregates, even when the tubes were agitated.

Discussion

Our findings show that in vivo regional stasis of blood in the left ventricle can produce an ultrasonic pattern that is distinct from left ventricular thrombosis. Distinct echocardiographic patterns appear to characterize intraventricular blood under conditions of normal flow, with severe regional stasis, and with thrombosis. When blood flow is normal, intracavitary ventricular blood does not produce a recognizable echogenic pattern when imaged with 3–5-MHz ultrasonic transducers; the blood is echolucent, despite the wide range of intraventricular pressures and flow velocities during the cardiac cycle. In the setting of severe regional ventricular dysfunction, especially at the cardiac apex, stasis of intracavitary blood occurs, and the acoustic properties of the blood in the area of dysfunction may produce a discernible echogenic pattern. A thrombus in the ventricle is an acoustically detectable mass with distinctive echocardiographic patterns.1–5

Several lines of evidence indicate that the in vivo intracavitary echo patterns seen in patients and in dogs are caused by stasis of blood. First, postmortem examination of the dogs showed only liquid blood to explain the echoes. Second, the intracavitary echoes are seen only in areas of altered blood flow. Both patients and dogs had severe regional dysfunction of the ventricular apex, evidenced by akinesis or dyskinesia in systole. In dogs, altered blood flow in the dysfunctional apical region could be deduced from the saline injections after coronary ligation. Postligation injections demonstrated relative persistence of echogenic contrast at the apex and circular motion of the contrast identical to that of the intracavitary echoes. Third, the configuration and motion of the intracavitary echoes indicate that their source is a fluid state, unlike the echocardiographic features of thrombosis.1–5 These intracavitary echoes show a dynamic variation in shape, conformation and acoustic density, even when they are acoustically intense and relatively homogeneous. Furthermore, alterations in ventricular contraction produced by ectopic beats, dopamine infusion, or mechanical external contraction lead to rapid changes in the configuration and density of the echoes. Last, static blood is echogenic. Normally echoluent blood becomes strikingly echogenic with the induction of mechanical asystole before postmortem clot formation. Our in vitro water bath studies and the studies of Sigel et al.2 also demonstrate the echogenicity of static blood.

An important finding in this study is the ability of real-time two-dimensional echocardiography to distinguish in vivo intraventricular blood stasis from thrombosis. Endocardial left ventricular thrombi have char-
acteristics of a definite mass on two-dimensional echocardiograms, are acoustically distinct from underlying myocardium, and have distinct margins. Although blood stasis without thrombosis may sometimes have sufficient acoustic intensity and uniformity to simulate a thrombus (fig. 3A), real-time imaging over several cardiac cycles or after ectopic contractions demonstrates obvious changes in the configuration and acoustic uniformity of these echoes and indicates a fluid state. Even the tail-shaped mobile red thrombi seen in some group 1 dogs could be distinguished from static blood. These red tails have been described as components of intraarterial thrombi and may represent rapid propagation of thrombus in an area of low blood flow. Although less acoustically intense than endocardial-based thrombi, the red thrombi had distinct margins (fig. 2A) that remained intact over long periods of time and after ectopic contractions.

The changes that occur in blood in areas of stasis and cause it to become echogenic are unclear. In vitro evidence suggests that certain components of static blood are echogenic while others are not. Sigel et al. demonstrated that whole blood, but not plasma and serum, is echogenic in vitro. Erythrocytes suspended in plasma, but not in serum or in saline, produce visible echoes. Our in vitro experiments support these findings and provide evidence that platelet aggregates are probably not the source of blood echogenicity. Neither platelet-rich plasma nor epinephrine-induced platelet aggregates produced echoes in a static state or after mechanical agitation that could be detected with a medium-frequency (5-MHz) transducer. The echogenicity of blood components may also depend on factors related to blood flow, including rheologic and biochemical properties, and changes in the physical alignment of potentially echogenic blood components in the area of blood stasis. Sigel et al. postulated that physical layering of static blood might be an important consideration in its echogenicity. Our observations support the plausibility of this hypothesis in the in vivo functioning left ventricle. The circular motion of blood in the abnormal apical segment may result in a more orderly and repetitive interaction of blood elements than normally occurs, thereby enhancing the physical alignment of potentially echogenic blood elements. The persistence of blood in the dysfunctional apex, which could be deduced from the contrast injections, would augment this process.

We have not observed the echocardiographic pattern of blood stasis in patients in regions of the left ventricle other than the apex (table 1). Nevertheless, with a ventricular aneurysm of a nonapical wall, including diastolic as well as systolic myocardial bulging, stasis of blood should be severe and therefore potentially echogenic. The apical segment of the ventricle, however, may be uniquely predisposed to severe blood stasis after ischemia, even in the absence of clear-cut aneurysm. Left ventricular thrombi show a predilection for the cardiac apex, and theoretical considerations indicate that the apex may be particularly susceptible to increased wall stress and changes in regional conformation after ischemia. In a prospective study of left ventricular thrombus formation after a first myocardial infarction, apical systolic akinesis or dyskinesis was significantly related to left ventricular thrombus formation. The unique cup-like shape of the apex and its primary contribution to the long-axis systolic shortening of the heart may contribute to the predisposition of this region to blood stasis during ischemic dysfunction. Thus, blood adjacent to an akinetic, but nonaneurysmal, inferior wall might demonstrate less derangement of flow during the cardiac cycle because of the influence of a normally contracting anterior free wall or apical segment. In contrast, akinesis of the apex produces isolation of the blood in this region, and other normally contracting proximal ventricular walls cannot affect the blood in this area as profoundly.

Our findings support the hypothesis that the more severe the degree of blood stasis present, the more pronounced the changes that lead to blood echogenicity; however, intraventricular stasis of blood cannot be quantitated. The degree of left ventricular dysfunction caused by general anesthesia, for example, did not lead to echogenicity of the intracavitary blood. Ischemically induced severe regional dysfunction, however, produced regional echogenicity, while complete mechanical asystole led to a diffuse echogenicity of the ventricular contents. There may well be a variable and nonlinear relationship between the degree of blood stasis and blood echogenicity. Different blood types, erythrocyte concentrations, or species might have different "thresholds" of stasis at which blood becomes echogenic. Investigation into this area will require development of models or methods for quantitating blood stasis in the dysfunctional ventricle, where flow patterns are more complex than in peripheral vessels.

Technical aspects of the echocardiographic examination and the ultrasonic frequency are also important considerations in a study of the acoustic properties of blood. These factors, as well as the biologic factors noted above, may explain why many patients and some of the dogs did not show echocardiographic evidence of blood stasis despite qualitatively similar degrees of left ventricular dysfunction. Clinical two-dimensional echocardiographic imaging in adults is generally done with 3.0–3.5-MHz transducers. Higher frequency transducers might enhance the ultrasonic demonstration of blood stasis. The echocardiographic patterns of flow stasis in the dogs were more easily seen with a 5-MHz than with a 3-MHz transducer. In patients with apical wall motion abnormalities, a 5-MHz transducer can be used in the apical acoustic window because the transducer is near the heart. We have used this approach in patients to confirm the echo pattern of blood stasis when it was only suggested with a lower frequency transducer.

Our studies have several clinical implications. The detection of blood stasis at the apex may identify patients at increased risk of developing left ventricular thrombus. Whether echocardiographic detection of regional stasis without thrombosis should lead to a con-
sideration of prophylactic anticoagulant therapy remains to be studied. In patients who have thrombi that disappear after anticoagulant therapy, persistence of echocardiographic evidence of blood stasis might indicate the need for long-term anticoagulant therapy. Our data do not allow us to draw conclusions on this possibility. Further, blood stasis could be mistaken for thrombosis when the echo pattern is relatively intense. Failure to distinguish thrombosis from blood stasis could affect echocardiographic studies on the natural history or response to therapy of left ventricular thrombi. Careful real-time echocardiographic study of the echoes after extrasystolic beats or hemodynamic interventions might be considered in uncertain cases. Finally, the ability to detect regional blood stasis in vivo by echocardiography further demonstrates that the acoustic impedance properties of early blood thrombosis can be detected ultrasonically.

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