Abnormal Blood Pathways in Left Ventricular Cavity in Acute Myocardial Infarction

Experimental Observations With Special Reference to Regional Wall Motion Abnormality and Hemostasis

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To elucidate the mechanism of regional hemostasis in the left ventricular (LV) cavity during myocardial infarction, the blood pathway in LV cavity was examined with contrast echocardiography injected from the left atrium before and after coronary ligation in nine canines. Before coronary ligation, contrast echoes spread over LV cavity with one rush. After ligation, smokelike echoes indicating hemostasis were observed at the apical middle of the LV cavity in five dogs with apical akinesis and at the apical area in four dogs with apical dyskinesis. The contrast echoes did not reach the apex within one diastolic period but turned upward to the outflow tract in the middle of the cavity in all dogs. In the cardiac beats that followed, some contrast echoes spread slowly toward the apex, forming a thin layer along the posterior wall in cases with akinesis but not in cases with dyskinesis. The area separated from the blood pathway developed where the smokelike echoes had been developed. Tachycardia exaggerated the abnormality of blood pathway and widened the contrast echo-free area. The abnormal pathway of the blood in apical myocardial infarction develops hemostasis in the apex. This should be one of the mechanisms of thrombus formation in myocardial infarction. (Circulation 1988;78:157-164)

Left ventricular (LV) mural thrombus formation is a major complication in myocardial infarction. Its incidence is especially high in patients with apical aneurysm. Also, rapid thrombus formation is characteristic after the onset of myocardial infarction.1-4 Although the mechanism of thrombus formation is not always apparent, hemostasis must be the most important factor for it. Recently, it has been noted that hemostasis can be observed by echocardiography as smokelike echoes.5-8 Smokelike echoes are frequently observed in clinical and experimental cases of myocardial infarction, especially in the infarct region.9-11 A high incidence of thrombus has also been proven in cases with such echoes. Although hemostasis can be observed as smokelike echoes, the mechanism of regional hemostasis in acute myocardial infarction has not been elucidated. Regional hemostasis in the LV cavity may be defined as uneven flow or little exchange of blood in the area concerned. To elucidate the mechanism of regional hemostasis from this definition, we studied the pathway of the inflow blood using contrast and Doppler echocardiographies in experimentally induced acute myocardial infarction. The influence of the velocity of the inflow blood, the maximum distance of inflow blood toward the apex in one diastole, the severity of the regional wall motion abnormalities, and the heart rate were also examined.

Materials and Methods

Nine mongrel dogs, weighing from 14 to 32 kg, were anesthetized with intravenous administration of 10–15 mg/kg pentobarbital and ventilated with a positive pressure respirator (Bird Mark 7, Palm Springs, California). Thoracotomy was performed along the seventh left intercostal space. Myocardial infarction at the apex was induced by ligating the coronary arteries until they had almost the same infarcted size. Because of variation in the distribution of the coronary arteries among the dogs, all branches of the left anterior descending and circumflex arteries were ligated in the apical
one third of the ventricle. If the asynergic area assessed by two-dimensional echocardiographic apical long-axis view was obviously less than one third of the LV, additional proximal sites of the coronary arteries were ligated. To avoid ventricular arrhythmia, 0.8–1 mg/kg lidocaine was injected intravenously before ligation. All examinations were performed before and 1 hour after the coronary ligation. Heart rate was controlled by right atrial pacing. It was elevated stepwise at a rate of 10 beats/min above the natural rate until atrioventricular block occurred. During the echocardiographic recordings, the respirator was turned off so that the diastolic filling should not be influenced by positive pressure respiration.

Echocardiography

The echocardiograph was an electronic phased-array system fitted with a pulsed-Doppler unit, Hewlett-Packard model 77020 AC (Andover, Massachusetts), with a 5 MHz shallow-focused transducer. Real-time two-dimensional echocardiograms were recorded by a video tape recorder (BR-6400, Victor, Yokohama, Japan) for frame-by-frame analysis. The transducer was placed at the cardiac apex to observe the conventional apical long-axis view of the LV (Figure 1). The ultrasound beam for M-mode echocardiography was directed to the coaptation point of the anterior and posterior mitral leaflets. M-mode echocardiograms and pulsed-Doppler echocardiograms were recorded by a strip-chart recorder (model 77500C, Honeywell, Andover, Massachusetts) at a paper speed of 50 mm/sec. The end-diastolic long axis of the LV was measured as the distance from the coaptation point of the mitral valve to the apex on the M-mode echocardiogram (Figure 1).

Contrast Study

A narrow vinyl tube, 2.5 mm i.d., was inserted into the left atrial cavity through the left appendage. The contrast medium, 2 ml saline agitated with carbon dioxide, was injected for a few seconds into the left atrial cavity through the vinyl tube. Special care was taken to avoid any irregularity in injection. The contrast study was performed in duplicate or triplicate at each pacing rate. Contrast echoes were recorded simultaneously by both two-dimensional and M-mode echocardiographies. The maximum distance of inflow of contrast echoes from the mitral orifice toward the apex in one diastole was measured with the M-mode echocardiogram (Figure 1). If the line of the contrast echo was broken or was too vague to analyze, the contrast study was performed again. The statistical value was obtained by averaging the measurements of three cardiac beats. Two-dimensional patterns of the spread of contrast echoes in the LV cavity were analyzed by reviewing the two-dimensional images on each frame of the videotape. Special attention was paid to the mode of spread of the bolus of contrast echoes into the LV.

Doppler Measurements

The position of the transducer and the direction of the ultrasound beam for pulsed-Doppler echocardiography was the same as that mentioned above. The sample volume was set at the coaptation point of the anterior and posterior mitral leaflets at end systole. Peak velocity of the inflow blood at both the rapid-filling period and at atrial contraction were measured. LV filling period was determined as the interval from the onset of the rapid-filling wave to the termination of the atrial contraction wave (Figure 1). If the beginning or end of the Doppler signal was not obvious, an intercept of the acceleration or deceleration was used, respectively. Each value was obtained by averaging the measurements of three cardiac beats.

Assessment of Wall Motion Abnormality

The severity of the wall motion abnormality was assessed by two-dimensional echocardiography on
Table 1. Relation Between Severity of Wall Motion Abnormality, Site of Smokelike Echoes, Mode of Spread of Contrast Echoes, and Development of Thrombi

<table>
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<th>Smokelike echo</th>
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<th>Turn flow</th>
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Wall motion, wall motion of the apex; Smokelike echo, site of smokelike echoes; Contrast, mode of the spread of contrast echoes; Turn flow, flow turned to the outflow tract in the middle of the inflow tract; Into apex, inflow to the apex; Thr, thrombus formation; A, akinesis; D, dyskinesis; center, center part of the left ventricular (LV) cavity; ant, anterior part of the LV cavity; apex, apex part of the LV cavity; ±, tiny flow forming very thin layer.

a three-grade scale: normal, akinesis, and dyskinesis. Dogs showing akinesis in a large area, as well as dyskinesis in a small area, were rated as having akinesis and vice versa. The evaluation of the severity of the wall motion abnormality was performed by two independent examiners. If the evaluation was different between them, the echocardiograms were reviewed until a consensus was reached.

Definition of Smokelike Echoes
Localized and dense intracavitary echoes are defined as smokelike echoes as in the literature. Generalized and fine echoes are excluded.

Statistical Analysis
The difference in the statistical values obtained before and after coronary ligation was analyzed by paired t test, and a p value of less than 0.05 was accepted as statistically significant.

Results
Wall Motion Abnormalities and Smokelike Echoes
No dogs had wall motion abnormalities before coronary ligation. After ligation, the LV cavity was enlarged, and akinesis of the apex developed in five dogs and dyskinesis in four dogs (Table 1). Although two dogs showed both akinesis and dyskinesis in almost equivocal areas, they were classified according to the predominancy of its area. They are labeled as “A(D)” and “D(A)” in Table 1. Smokelike echoes were observed in all dogs. In dogs with apical akinesis, smokelike echoes curled slowly in the apical center of the LV cavity (Figure 2A). In dogs with apical dyskinesis, they were flame shaped or half-moon shaped in the apical area (Figure 2B).

As the echoes moved slowly toward the apex in systole, they showed a relatively rapid motion toward the cardiac base in diastole (Table 1).

Pathway of Contrast Echoes in Left Ventricular Cavity

Before coronary ligation. Contrast echoes from the left atrium reached nearly the apex in one diastole at the natural heart rate in every dog, spreading over the whole LV cavity, even into the outflow tract with the exception of a small area just beneath the aortic valve (Figure 3). An increase in the heart rate to about 100 beats/min resulted in the apical area not being filled by contrast echoes in one diastole so that the maximum distance of the inflow of contrast echoes became shorter than the long-axis of the LV. However, the shortening was so slight that the apical area was filled sufficiently during the following diastole (Figure 4A).

After coronary ligation. The maximum distance of the inflow of contrast echoes became significantly shorter after ligation in every dog. The higher the heart rate, the shorter was its distance (Figure 4B). The pathway of contrast echoes, however, depended on the severity of apical asynergy (Table 1). In every dog with apical akinesis, the contrast echoes did not fill the apical area within one diastole.
but separated into two streams in the middle of the inflow tract. One was the outer stream flowing toward the apex along the posterior wall, and the other was the inner stream taking a short cut to the outflow tract at the middle of the cavity (Figure 5). The outer stream flowed gradually toward the apex even during the following systole (Figure 5C), being pushed by new inflow blood in the subsequent diastoles (Figures 5C and 5D). Consequently, a slow but continuous blood flow formed along the apical wall, throughout the entire cardiac period. The inner stream of the contrast echoes met the outer stream again at the outflow tract, and they were ejected together (Figure 5C). Namely, the ventricular septal side of the outflow tract consisted of the blood slowly rounding along the apex, and the anterior mitral leaflet side consisted of the blood taking a short cut. In the apical center of the cavity, a contrast echo–free area developed, being enclosed by the two blood pathways described above (Figure 5D). This is the area where the smokelike echoes were visualized (Figure 2A). With an increase in pacing rate, the area of smokelike echoes became wider. The inner stream of contrast echoes immediately turned back toward the outflow tract, and the outer stream passing along the apical wall became thinner, resulting in a widening of the contrast echo–free area.

In cases with apical dyskinesis, almost all contrast echoes reversed their direction toward the outflow tract immediately after they entered into the LV cavity (Figure 6). The apical area, where smokelike echoes were observed, was barely filled with contrast echoes. The entry of the contrast echoes appeared to be hindered by the tidal motion of the smokelike echoes (Figure 7). The border between the area of both the smokelike echoes and the contrast echoes was sharp. Tachycardia increased the contrast echo–free area as did apical akinesis. An abnormal mass echo was detected at the apex in one dog with apical dyskinesis, and this was later confirmed as a blood clot in autopsy.
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FIGURE 5. Echocardiograms and schematics of blood pathway in a case of apical akinesis (same case as in Figure 3A). Arrow indicates the time of two-dimensional echocardiographic recording. Panels A and B: In the first diastole after injection, most of the contrast echoes turn back to the outflow tract. Panel C: In systole of the next beat, the contrast echoes turning back to the outflow tract are ejected with the "old" blood. Contrast echoes near the posterior wall partially enter the apical area along the posterior wall. Panel D: In the next diastole, the fourth diastole after injection, the contrast echoes move gradually to the apical area, but a contrast echo-free region is seen in the middle of the left ventricular cavity. Heart rate is 100 beats/min.

In additional experiments with small-sized asynchrony, abnormal spread of the contrast echoes was not obvious.

Other Variables

After the coronary ligation, natural heart rate increased from 78 ± 14 to 92 ± 12 beats/min. The long axis of the LV increased significantly from 49 ± 7 to 56 ± 6 mm (Figure 8). The Doppler signals at the rapid-filling period and atrial contraction tended to fuse to one another after ligation. Therefore, the effect of coronary ligation at the same heart rate could be evaluated in only six dogs. The maximum distance of the inflow of contrast echoes

FIGURE 6. Echocardiograms of blood pathway in a case of apical dyskinesis (same case as in Figure 3B). Panel A: In the first diastole after injection, most of the contrast echoes turn back to the outflow tract of the left ventricle. Panel B: In the next systole, contrast echoes near the posterior wall move toward the apex but do not flow into the apical region. Heart rate is 140 beats/min.
decreased from 46 ± 8 to 36 ± 6 cm. The peak velocity of the rapid-filling wave decreased significantly from 57 ± 20 to 34 ± 11 cm/sec, that of the atrial contraction also decreased from 36 ± 11 to 28 ± 7 cm/sec (Figure 8). Also, the effective-filling period became shorter from 300 ± 29 to 260 ± 33 msec even in the same heart rate. These decrements were statistically significant but were not different between dogs with apical akinesis and dyskinesis.

Discussion

Method for Assessing Dynamics of Blood

There are several methods for assessing the dynamics of the blood in the cardiac cavity. Although pulsed-Doppler echocardiography provides a precise temporal pattern of flow velocity at any site in the cavity, it is a pinpoint evaluation and requires a mapping technique to cover a wide area.12,13 Even color-coded two-dimensional Doppler echocardiography is a reconstructed image based on the flow velocity toward the transducer and not necessarily convenient for tracing a specified flow. On the other hand, contrast echocardiography is advantageous for tracing a specified flow, in that it traces the fate of a specified part of the blood on its pathway. However, it is difficult to calculate the statistical value, such as flow velocity, by the contrast technique. These were the reasons that contrast echocardiography and pulsed-Doppler echocardiography were used to analyze the dynamics of the inflow blood in the LV cavity.

Pathway of Blood

It was shown that the inflow blood spread widely almost over the whole LV cavity in one diastole in cases without wall motion abnormality. The inflow blood flows against the apex and turns toward the outflow tract. That is, most blood in the LV cavity shifts in one diastole.

In dogs with apical myocardial infarction, although the LV cavity is morphologically one space, the cavity functions as if composed of two parts with respect to the blood pathway: one part is for blood turnover, and the other part is separated from blood turnover. The degree of this abnormality of the pathway of blood probably depends on the size and type of asynergy of infarcted area. The cause of the variety of apical asynergy among dogs in the present study is not obvious. However, the long axis of the LV increased, and maximum velocities of inflow

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**FIGURE 7.** Echocardiogram of counterflow of the smokelike echoes and mode of inflow of the contrast echoes in a case of apical dyskinesis (same case as that in Figures 3B and 6). Smokelike echoes occupy almost apical half of the left ventricular cavity and move toward the cardiac base (downward large arrow) just before the mitral valve opening (upward small arrow). Contrast echoes are prevented from entering the apex. Apical wall is thin in systole. Heart rate is 110 beats/min.

**FIGURE 8.** Plots of changes of the variables of diastolic hemodynamics before (C) and after (L) coronary ligation at the same heart rate of 100 beats/min except long axis of the left ventricular cavity (LV). Open and closed circles indicate the case of apical akinesis and dyskinesis after coronary ligation, respectively. Max D, maximum distance of the inflow of contrast echoes; R, peak velocity of early diastolic phase; A, peak velocity of atrial filling phase; Diast time, effective filling time.
blood at early diastole and at atrial contraction phase and effective diastolic period decreased in all, without a significant difference between akinetic and dyskinetic dogs. Therefore, in dogs with relatively large infarcted area, there is not much doubt that distribution of the inflow blood to the apex depends on the severity of asynery of the apex. In apical akinesis, the inflow blood branches into two streams and the stagnant lump of blood develops between these two streams. In apical dyskinesis, distribution of the inflow blood toward the infarcted area is absent or extremely small, and blood stagnation develops in the apex.

The difference in the pathway of blood due to the severity of apical asynery is as follows. The blood near the apex is forced to the dyskinetic apical area during systole. Immediately after the end of systole, the forced blood returns, being the counterflow against the inflow blood. In the literature with Doppler echocardiography, there is a rapid flow toward the cardiac base at the isometric relaxation period in the case of apical infarction,13,14 which relates to the asynchronous relaxation.15–18 As the counterflow is not significant in cases of apical akinesis, part of the inflow blood seems to flow toward the apex along the posterior wall.

Although the apical wall motion abnormality seems to be essential in promoting the abnormal pathway of the inflow blood, other hemodynamic variables are also important as an underlying condition. Blood velocity of the early diastolic filling wave is slow in clinical and experimental myocardial infarctions.19–21 Also, in acute myocardial infarction, motion of the mitral valve on the M-mode echocardiogram tends to be monopeaked, indicating short effective filling period, because of prolongation of the isometric relaxation time.22 Combination of these changes and enlargement of the cavity size will promote the abnormality of pathway of blood.

It is a wonder that the blood along the posterior wall flows not only in diastole but also in systole. Its mechanism remains unclear. Additional investigations may be necessary to elucidate the influence of the extent of asynery and the compensatory motion of nonischemic region.

Clinical Significance

It has been revealed that stagnant blood becomes echogenic and that sluggish blood flow is observed as smoke-like echoes.5–11 As shown by the contrast study, a certain volume of the blood forms a lump separated from the functioning blood pathway, developing smoke-like echoes and sometimes resulting in clot formation.

It is supposed that the blood in the LV cavity generally turns over smoothly in tachycardia and tends to stagnate in bradycardia. However, this conception is quite reversed. Tachycardia may have to be controlled to prevent thrombus formation.

The present study was an experiment based on the assumption of acute myocardial infarction. LV thrombosis does not occur only in myocardial infarction but also frequently in a dilated LV with reduced wall motion as observed in dilated cardiomyopathy. In such a case, pathway of the blood in the LV cavity may be different from that in the present study. Further investigation is needed.

References


KEY WORDS • contrast echocardiography • Doppler echocardiography • thrombus • ventricular asynergy
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