Left atrial appendage Doppler flow patterns: Implications on thrombus formation

The characteristics and clinical implications of left atrial appendage (LAA) flow have not been clearly analyzed. Thirty-nine consecutive patients underwent a transesophageal echocardiographic (TEE) color Doppler study to correlate the LAA pulsed Doppler flow pattern with echocardiographic variables and the cardiac rhythm of each patient. Three different LAA flow patterns were identified. Type I flow, characterized by a biphasic pattern (waves of filling and emptying), was found in 17 patients, all in sinus rhythm; it was not associated with LAA spontaneous contrast or thrombus. Mean peak velocities of the filling and emptying waves were, respectively: 28 ± 12 cm/sec and 31 ± 9 cm/sec. Type II sawtooth active flow (eight patients) (mean peak velocity: 49 ± 12 cm/sec) was only detected in atrial fibrillation (AF) and dilated LAA (LAA area: 421 ± 40 mm^2) but without thrombus or significant LAA spontaneous echocardiographic contrast. Type III flow pattern was noted in 14 patients with AF and a very dilated LAA (LAA area: 619 ± 96 mm^2). This flow pattern was characterized by the absence of identifiable flow waves and was associated with the presence of LAA spontaneous contrast; the majority (six of seven) had evidence of thrombus. We concluded that the LAA is a dynamic structure in which TEE study identified three flow patterns with different implications. AF is associated with two LAA flow types (II and III) with a larger LAA size as well as a higher incidence of LAA clots in type III flow. (Am Heart J 1992;124:955.)

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Two-dimensional echocardiography is a well-established technique in the assessment of left atrial anatomy and in the diagnosis of left atrial masses. However, the left atrial appendage (LAA) is the only cardiac structure that remains difficult to examine thoroughly by the precordial approach.[1, 2] However, transesophageal echocardiography (TEE) provides highly accurate images of the left atrium and particularly of the LAA.[3-7] This technique is currently used for the assessment of left atrial spontaneous echocardiographic contrast and LAA thrombi and their relationship, together with the clinical outcome.[4-11] The predilection of the LAA for thrombus development is well known. However, the characteristics and possible clinical implications of LAA flow still remain to be clearly analyzed. Our study was directed at assessing by means of TEE the characteristics of the dynamic flow of the LAA and its possible relationship to left atrial dimensions and the presence of left atrial and LAA spontaneous contrast and clots, as well as determining the cardiac rhythm of the patient.

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METHODS

The study group consisted of 39 consecutive patients (11 men and 28 women; mean age 56 ± 23 years) who underwent a TEE study in our laboratory. At the study, 18 patients were in sinus rhythm, whereas the remaining 21 patients showed atrial fibrillation. The reasons for the study were: the assessment of rheumatic valve disease (27 of 39; 69%); the evaluation of prostheses (4 of 39; 10%); the determination of mitral valve prolapse (2 of 39; 5%) and cardiomyopathy (2 of 39; 2.6%); and the investigation of the embolic source (4 of 39; 13%). Before the transesophageal evaluation, all patients underwent a complete transthoracic study (two-dimensional, spectral pulsed- and continuous-wave Doppler, and color flow Doppler studies) using a commercially available Doppler echocardiography unit (Sonos 1000, Hewlett-Packard Co., Medical Products Group, Andover, Mass.) with a 3.5 MHz phased-array transducer. Transthoracic two-dimensional echocardiographic examinations were performed following conventional criteria. Left atrial area was measured by planime-

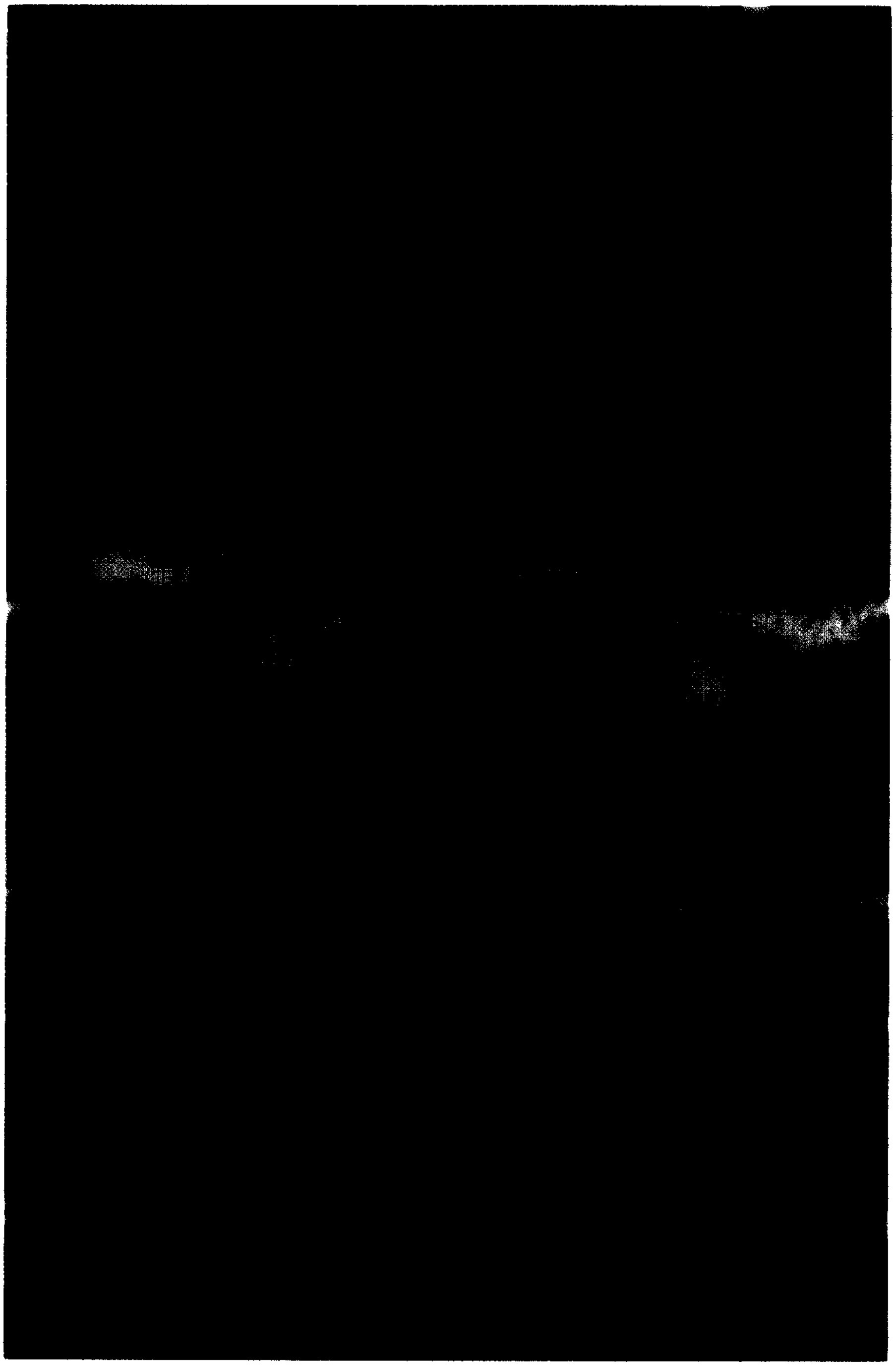

Fig. 1. Type I LAA Doppler flow pattern with well-defined emptying and filling waves *(arrows in the upper figure)*. The sample volume is placed in a small LAA cavity. The color-coded study across the LAA demonstrates the corresponding red emptying and blue filling Doppler flow *(arrows in the lower panel).*

try of the endocardial borders of this structure as obtained from the apical four-chamber view.

Subsequently the TEE study was performed in each patient after topical anesthesia of the hypopharynx and mild sublingual sedation with diazepam (10 mg). All studies were carried out by two experienced cardiologists using a 5.0 MHz transducer mounted at the end of a 100 cm echoscope. The echoscope was advanced 25 to 30 cm from the incisors, and superior tilting of the tip of the echoscope allowed consistent imaging of the left atrial appendage at a basal short-axis view.[3] The total area of the LAA was measured with a trackball by tracing the endocardial borders of this triangular extension of the left atrial cavity, and the area was calculated by computed planimetry. In each case,

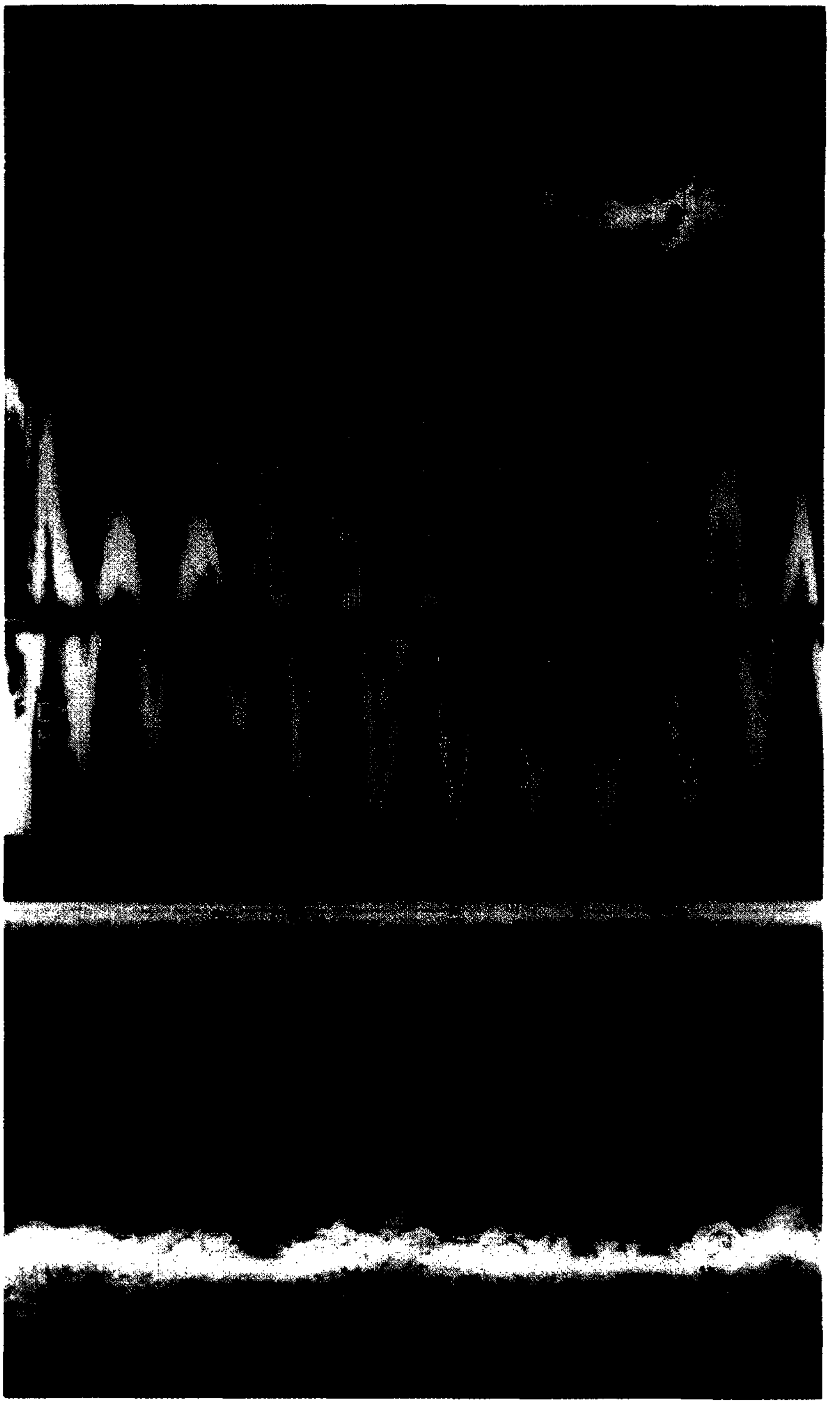

Fig. 2. Type II LAA flow pattern with an active "sawtooth" flow profile *(arrows in the upper figure).* The color-coded study across the LAA shows the corresponding bright red emptying and blue filling Doppler flow *(arrows in the lower panel).*

the maximum LAA area obtained was included in the analysis. In the patients who were in sinus rhythm, the maximum LAA area at the onset of the P wave was measured. In the patients in atrial fibrillation (AF), this maximum area was determined independently of the electrocardiogram. The perimeters of the LAA extended from the apex to the base of the limbus between the upper left pulmonary vein and the LAA and a perpendicular straight line drawn to the aorta. Clots were defined as echo-dense masses within the LAA. Special care was taken in differentiating LAA clots from muscular ridges (pectinate muscles). Spontaneous dynamic contrast was defined as the presence of swirling smoke-like echoes within the left atrium or the LAA, using appropriate gain settings. Finally,

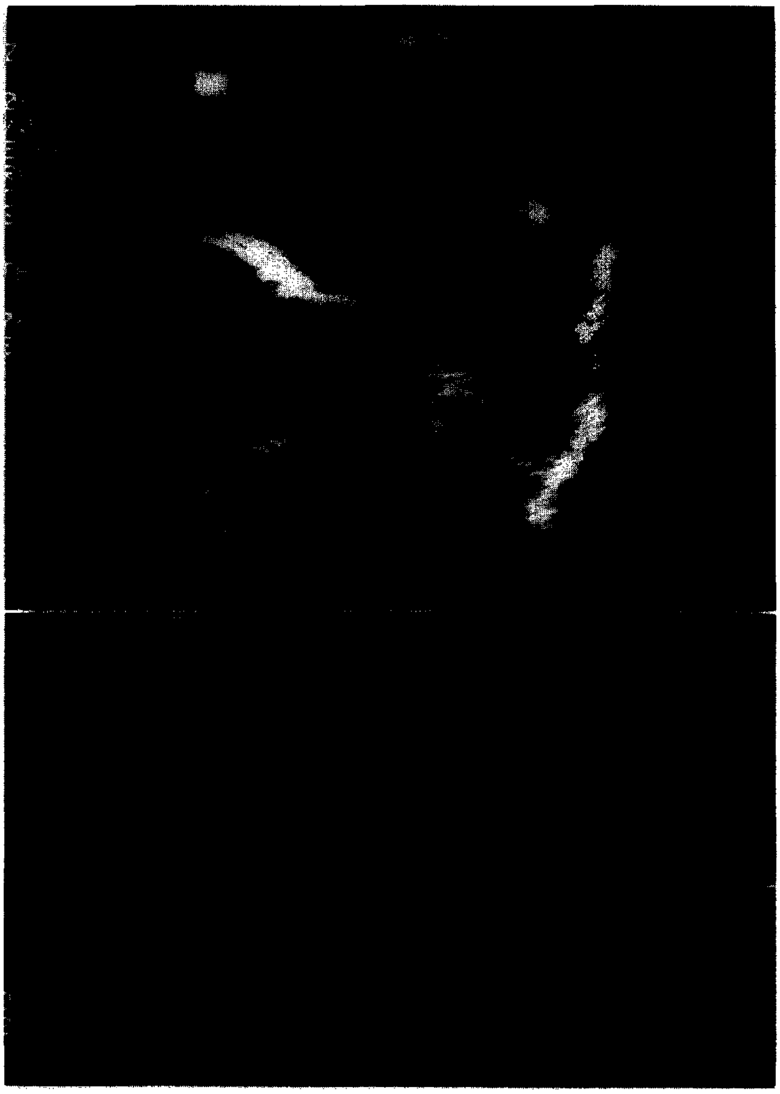

Fig. 3. Type III LAA Doppler flow pattern with a very low profile. The sample volume is placed in the LAA. Note the enlarged LAA cavity associated with this Doppler flow pattern. One can observe the presence of discrete sharp signals during the inscription of QRS deflections, corresponding to wall noise artifacts. No LAA color-coded flow was registered. *LA,* Left atrium; *SV,* sample volume; *AO,* aortic root.

pulsed-wave and color Doppler studies of the LAA flow were obtained in every patient. The sample volume was placed within the LAA body near the base of this structure and equidistant from both LAA walls. In each case we measured peak velocity and the area enclosed in the spectral tracing of the LAA filling and emptying Doppler waves. The values of three and five measurements were averaged in patients with sinus rhythm and AF, respectively. All studies were reviewed independently by two experienced observers with respect to the type of LAA flow and the presence of LAA clots and atrial spontaneous contrast; any discrepancy was resolved by consensus.

Statistical analysis. Values are reported as means ± 1 SD. Chi-square tests were used to compare categorical variables. One-way analysis of variance was used to compare continuous variables between groups, with a subsequent Scheffé test for multiple means comparisons. Statistical significance was defined as a two-tailed $p < 0.05$.

RESULTS

Three different flow patterns were identified within the LAA. Type I flow was characterized by a biphasic flow of clearly defined waves of filling and emptying (Fig. 1). On the other hand, in type II flow a characteristic "sawtooth" morphology of fast, well-defined flow waves was noted (Fig. 2), whereas in type III flow there were no identifiable flow waves in the LAA by Doppler testing (Fig. 3).

Type I flow was present in 17 (43%) patients and all of them showed sinus rhythm. The prevalence of the different etiologies was: rheumatic mitral disease (eight patients); mitral prosthesis (two patients); mitral valve prolapse (two patients); dilated cardiomyopathy (one patient); finally four patients were studied for detection of cardiac source of embolism.

Table I. Cardiac rhythm and electrocardiographic data of the patients according to LAA flow pattern

	LAA flow type			
	I	*II*	*III*	*p Value*
Patients (n)	17	8	14	—
Atrial fibrillation	0/17	8/8	13/14	<0.001
LA spontaneous contrast	3/17	5/8	12/14	<0.001
LAA spontaneous contrast	2/17	2/8	12/14	<0.001
LAA thrombus	1/17	0/8	6/14	<0.02
LA area (cm^2)	20.1 ± 5.2	26.6 ± 5.5	35.8 ± 11.2	<0.005
LAA area (cm^2)	3.3 ± 6.4	4.2 ± 4	6.2 ± 9.6	<0.001

LA, Left atrial; *LAA*, left atrial appendage.

Mean peak velocities of the filling and emptying waves were: 28 ± 12 cm/sec and 31 ± 9 cm/sec, respectively. The area enclosed by the filling wave averaged 514 ± 260 mm^2 and the area under the emptying wave was 544 ± 200 mm^2. Type II flow was found in eight (20%) patients with atrial fibrillation, seven of them with mitral stenosis and one patient with dilated cardiomyopathy. The mean peak velocity of these bidirectional flow waves was 49 ± 12 cm/sec ($p < 0.005$). No distinct flow into the LAA was observed in 14 patients (type III flow); sinus rhythm was noted in just one of them, whereas the remaining 13 patients showed AF. Absence of active LAA flow was found in 12 patients with mitral stenosis and in two with a mitral prosthesis.

Left atrial spontaneous echocardiographic contrast was found in 3 of 17 (18%) patients with type I flow, in five of eight (62%) cases with type II flow, and in 12 of 14 (85%) with type III flow ($p < 0.001$). On the other hand, spontaneous contrast within the LAA was detected in 2 of 17 (11%) patients with type I flow, in two of eight (25%) with type II flow, and in 12 of 14 (86%) with type III flow ($p < 0.001$). Average LAA area was different in each of these flow types; thus mean LAA area in type I flow was 333 ± 64 mm^2, whereas this area averaged 421 ± 40 mm^2 in type II flow and 619 ± 96 mm^2 in type III flow ($p < 0.001$). Interestingly, we found LAA thrombus in seven patients, six of them with type III flow, and only one showed type I flow. Table I shows the relationship of the three different flow patterns with the correlated electrocardiographic and echocardiographic data.

DISCUSSION

Our data demonstrate that Doppler interrogation of the LAA dynamics can identify different flow patterns with implications on echocardiographic findings and on the cardiac rhythm of patients. The results of the present study indicate three different LAA Doppler flow patterns as assessed by the transesophageal approach and their relationship to cardiac rhythm, left atrial size, and the presence of both spontaneous echocardiographic contrast and LAA thrombi.

LAA Doppler flow pattern and electrocardiographic characteristics. Type I flow is found in patients with sinus rhythm. However, type II and III flow was present in patients showing AF. The fact that AF was associated with two LAA flow patterns could suggest the presence of two distinct types of this tachyarrhythmia, with different mechanical behavior and unique consequences on atrial blood stasis and thrombus development. Whether the latter could be related to classic differentiation of this arrhythmia based on fibrillation wave shape is outside the scope of this study. Nevertheless, the results of recent studies describing different types of AF based on the bipolar atrial electrogram morphology recorded during AF have shown a spectrum of organization of the atrial electrogram potentials.[12, 13] The possible correlation of these electrophysiologic patterns of AF with the two types of LAA flow observed in our patients with this arrhythmia would require further studies. On the other hand, the duration of this arrhythmia was not taken into account in our study, and we can not exclude the possible implication of this factor on LAA dynamics.

LAA Doppler flow pattern and the presence of LAA thrombus. It is well known that dilated and adynamic myocardial wall segments, like ventricular aneurysms, have low Doppler flow areas with a strong correlation with local thrombus formation. Recently, Daniel et al.[11] established a clear relationship between left atrial spontaneous contrast and the presence of left atrial thrombi. In our study, the absence of identifiable flow in patients with a type III flow pattern may predispose to blood stasis and clotting. In fact, we found that a type III Doppler flow pattern closely correlated with the presence of LAA thrombi. The only case with an LAA thrombus and type I flow pattern was a patient with a mechanical mitral prosthesis in sinus rhythm but without surgical resection of the LAA.

Our results suggest that absence of flow or very low

LAA Doppler flow probably play an important role in thrombus formation through blood stasis and spontaneous intracavitary echo contrast development.[11, 14-16] In fact, the type III flow group had the highest prevalence of left atrial and LAA echo contrast, as well as the highest incidence of thrombus. Recently, Pollick and Taylor[17] concluded that thrombus formation within the LAA in patients in sinus rhythm and with AF is associated with both a dilated and poorly contractile LAA, as determined by the ejection fraction of this structure calculated as $(LAA_{max} - LAA_{min})/LAA_{max}$. Moreover, these investigators precisely define the characteristic pattern of filling and emptying in sinus rhythm. However, the LAA Doppler pattern was only demonstrated in 10 of the 19 patients with AF.[17] On the contrary, our study only focuses on the LAA Doppler findings and further identifies this flow pattern in our 22 cases with AF.

Our study has a major limitation that requires some comment. The anticoagulation status of our patients is not given in this study, and it is known that treatment with anticoagulating agents is effective in the primary prevention of thromboembolic events in AF.[18] However, it is of interest that recent studies[8, 10] did not find anticoagulant therapy to be an independent factor related to the presence of left atrial thrombus.

LAA Doppler flow pattern and anatomic correlations. We observed that patients with the type I flow pattern had the smallest LAA dimensions. On the other hand, patients with type II or III flow both showed AF but a completely different two-dimensional echocardiographic anatomy. Furthermore, patients with type II flow showed only slight LAA dilation compared with those with type III flow who showed severe overall dilatation. Probably a greater LAA dilatation is associated with a poorer contractile ability of this structure. This relationship between anatomy and function is revealed through the absence of a dynamic Doppler flow in patients with a type III flow pattern. Patients with a type III flow pattern frequently showed larger LAA dimensions with loss of normal LAA contractility and a very low Doppler flow profile, signs of blood stasis, and thrombus formation. In our opinion, it is possible that type II flow pattern corresponds to an intermediate stage in which AF is present with an abnormal but still efficient Doppler flow profile in a mildly dilated LAA free of LAA spontaneous echocardiographic contrast.

TEE is currently considered the procedure of choice in the evaluation of LAA clots. However, the natural history of LAA thrombi needs to be prospectively evaluated before this finding should modify the decision-making process involving the prescription of anticoagulant therapy.[6] Furthermore, although spontaneous echoes are occasionally identified with transthoracic two-dimensional echocardiography,[14, 15] the awareness of this phenomenon has increased since the advent of TEE.[8-11, 17] The clinical significance of this finding with respect to both atrial clots and embolic events still remains controversial.[15, 16, 19] Finally, our results suggest that there are two types of AF with respect to LAA dynamics and thrombus formation. More studies are needed to ascertain whether these findings might restrict anticoagulant therapy to certain types of AF in specific clinical settings.

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The relationship between intracardiovascular smoke-like echo and erythrocyte rouleaux formation

Intravascular smoke-like echo always appears in regions of stasis, but the exact mechanism of its production is unclear. We investigated its appearance in relation to erythrocyte rouleaux formation. To study this relationship we performed a series of in vitro and animal experiments. In the in vitro study, we observed an erythrocyte suspension by ultrasonography and found it to be echo-free. Under the microscope, red blood cells were observed in a dispersed state. If an equal amount of lymphocyte separation solution was added to the suspension, smoke-like echo appeared, and red blood cells were seen in a rouleaux pattern. In animal (mongrel dogs) experiments, under physiologic conditions with normal blood flow velocity, all cardiac cavities and the inferior vena cava were echo-free. When stasis was induced experimentally in the inferior vena cava, red blood cells aggregated to form rouleaux and smoke-like echo appeared. On resumption of normal blood flow, the rouleaux dispersed to form erythrocytes again. The mechanism of production of intracardiovascular smoke-like echo is closely related to the formation of erythrocyte rouleaux. When rouleaux are formed, they become larger and appear nearer or larger than the ultrasonic wavelength. Thus reflections are produced and smoke-like echo appears. (AM HEART J 1992;124:961.)

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Intracardiovascular smoke-like echo, also called spontaneous echo contrast, is a phenomenon that usually appears in regions of stasis of blood flow; however, the mechanism of this phenomenon remains unclear.[1-5] Recently, after performing in vitro studies and animal experiments, we found that the appearance of smoke-like echo was closely related to erythrocyte rouleaux formation. This article discusses the studies, results, interpretations, and clinical implications.

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METHODS

An Aloka SSD-870 (Aloka Co., Ltd., Tokyo, Japan) Doppler color flow imaging system was used. Transducers used were Aloka UST-5227 with a frequency of 3.5 MHz and UST-5233-5 with a frequency of 5.0 MHz. Experimental specimens included (1) normal saline solution, (2) lymphocyte separation solution, which contains mainly Ficoll (macromolecular polymer) (Pharmacia, Inc., Piscataway, N.J.) but no visible component, and (3) erythrocyte suspensions of 40% to 50% specific volume made of human banked blood or canine anticoagulated blood, which was washed with normal saline solution by low-temperature centrifugal sedimentation (3000 turns/min for 10 minutes three times).