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Clinical Significance of Perfusion Imaging of the Left Atrial Wall and Structures in its Cavity by Contrast Echocardiography

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Abstract

This study examined whether myocardial contrast echocardiography (MCE) can visualize left atrial appendage myocardial perfusion using transesophageal echocardiography (TEE) with intracoronary injection of sonicated albumin. We also evaluated blood flow into normal structures (*i.e.* muscular trabeculae) and abnormal masses (*i.e.* fresh thrombi and myxomas) within the left atrium by MCE.

TEE images were obtained with a biplane or multiplane 5 MHz transducer in 16 patients without significant coronary artery occlusive disease. Left atrial appendage myocardium was divided into 4 segments in both the transverse and longitudinal planes, and contrast opacification of each segment during MCE was visually evaluated by 2 independent observers. Visual assessment of contrast opacification of prominent muscular trabeculae within the left atrial appendage (6 patients), and of left atrial or left atrial appendage thrombi (4 patients), was also performed. The ratio of background-subtracted peak videointensity from muscular trabeculae or thrombi versus left atrial appendage myocardium was determined as corrected peak videointensity. In 3 patients with myxomas, contrast opacification of the tumor was visually assessed.

Ninety-six segments of left atrial appendage myocardium were visually analyzed. Contrast opacification of the left atrial appendage myocardium was identified in 92 of 96 segments (96%, 95% confidence interval 0.90–0.98) by Observer 1 and in 91 of 96 segments (95%, 95% confidence interval 0.88–0.98) by Observer 2. MCE also enhanced the imaging of left atrial appendage muscular trabeculae, but not of left atrial or left atrial appendage thrombi. Corrected peak videointensity from thrombi was significantly lower than that from muscular trabeculae (0.15 ± 0.11 vs 0.95 ± 0.18, $p < 0.05$). All myxomas were distinctly opacified by MCE.

Transesophageal MCE with intracoronary injection of sonicated albumin can image left atrial appendage myocardial perfusion. MCE allows the evaluation of blood flow into normal structures and abnormal masses within the left atrium.

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Key Words

■ Contrast echocardiography ■ Coronary microcirculation
■ Echocardiography (transesophageal) ■ Thrombosis

INTRODUCTION

Transesophageal echocardiography (TEE) is used in the detection of left atrial thrombi, particularly left atrial appendage thrombi, because of its high resolution[1-4]. However, muscular trabeculae within the left atrial appendage or dense spontaneous echogenic contrast may occasionally be confused with thrombotic material[2,4].

The spatial distribution of the ventricular myocardial blood flow can be visualized by myocardial contrast echocardiography (MCE)[5-7]. However, since the atrial myocardium is considerably thinner than the left ventricular myocardium, it is not known whether MCE can visualize atrial myocardial perfusion. Imaging of atrial myocardial perfusion by MCE might provide a new method for the assessment of atrial structures. Therefore, this study was performed to examine the use of transesophageal MCE, with intracoronary injection of sonicated albumin microbubbles, to image left atrial appendage myocardial perfusion. We hypothesized that imaging of left atrial appendage myocardial perfusion showing the absence of arterial supply to fresh thrombi could allow the distinction between muscular trabeculae and thrombi by MCE. This also allowed us to evaluate blood flow into normal structures (*i.e.* muscular trabeculae) and abnormal masses (*i.e.* fresh thrombi and myxomas) within the left atrium by MCE.

SUBJECTS AND METHODS

Subjects

The study population comprised 8 men and 8 women, aged 37 to 77 years old (mean age 64 years), who underwent coronary angiography for various indications, including angina pectoris (2 patients), old myocardial infarction (2 patients), hypertrophic cardiomyopathy (one patient), dilated cardiomyopathy (one patient), myocarditis (one patient), mitral stenosis (3 patients), aortic stenosis (one patient), mechanical prosthetic valve (one patient), second-degree atrioventricular block (one patient), and left atrial myxoma (3 patients). No patient had significant angiographically visible occlusive coronary artery disease, including the 2 patients with histories of myocardial infarction who had undergone reperfusion therapy. Six patients had atrial fibrillation at the time of MCE. One patient had left atrial and 3 patients had left atrial appendage thrombus-like echocardiographic findings detected on previous TEE, and one of them had a history of cerebral thromboembolism. The final diagnosis of thrombi was based on changes in their size or shape over time. The histologic diagnosis of left atrial myxomas was made postoperatively. Informed consent to participate in the study was obtained from each patient.

Protocol

After the completion of diagnostic coronary angiography via the femoral approach, TEE was performed with the patient in a supine position, under sedation with intravenous diazepam, 5−10 mg, and topical anesthesia with 2% lidocaine jelly. Atropine sulfate, 0.5 mg, was administered intramuscularly, as necessary, to suppress salivation. TEE images were obtained with a commercially available phased-array system (EUB-555, Hitachi and SSD-2200, Aloka) with a conventional biplane or multiplane 5 MHz transducer, and were recorded on 1.25-cm videotape with a S-VHS recorder (AG-7355, Panasonic and SVO-9500MD, SONY).

Two m*l* of sonicated albumin were injected into the left and right coronary arteries through a 5 F Judkins' catheter for MCE imaging. Left atrial appendage images obtained in transverse and longitudinal plane views were recorded on videotape at a constant gain setting, beginning approximately 5 sec before the injection of the contrast agent, and ending when the contrast enhancement was no longer visible. MCE was repeated more than once in the same view to verify reproducibility. Lead II of the surface electrocardiogram was continuously monitored during and after MCE. The left atrial appendage myocardial contour was divided into 4 segments in both the transverse and the longitudinal planes (**Fig. 1**), and contrast opacification of each segment was visually evaluated by 2 independent observers (Observer 1 : T.A. and Observer 2 : M.O.). In addition, a visual assessment was performed of the contrast opacification of muscular

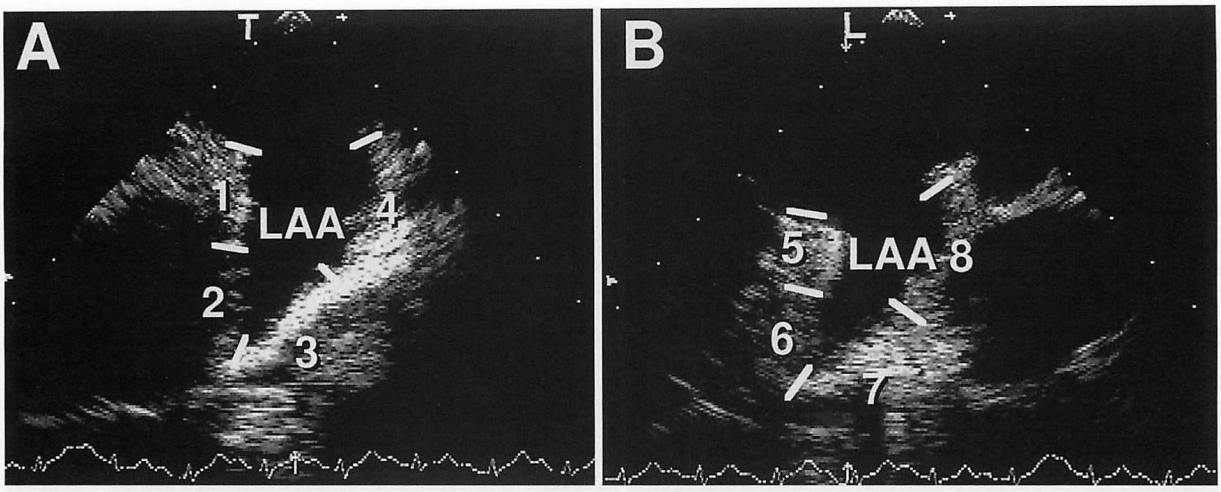

Fig. 1 Division of the left atrial appendage contour in 8 segments in the transverse (*A*) and longitudinal (*B*) planes
Contrast opacification of each individual segment was visually evaluated.
LAA = left atrial appendage.

trabeculae within the left atrial appendage and left atrial, or of left atrial appendage thrombi. In patients with prominent muscular trabeculae or thrombi, background-subtracted peak videointensity from muscular trabecula or thrombus, and from left atrial appendage myocardium were measured off-line from videotape images obtained in atrial diastole. The ratio of peak videointensity from muscular trabecula or thrombus and from left atrial appendage myocardium was determined as corrected peak videointensity. Gray scale software (SAS-200, Aloka) which measures videointensity (0 to 255 scale) versus time was used to measure the contrast intensity. The maximum size region of interest was set in the center of the muscular trabecula or thrombus for measuring the gray level, and the region of interest of adequate size for the left atrial appendage myocardium was also set in the contrast-opacified segment as reference. In patients with left atrial myxoma, contrast opacification of the myxoma was also visually assessed.

Statistical analysis

Ninety-five percent confidence intervals (CI) were calculated based on a normal distribution. All data are expressed as mean ± standard deviation. Comparisons of corrected peak videointensity between muscular trabeculae and thrombi were assessed by the Mann-Whitney *U*-test. A p value < 0.05 was considered statistically significant.

RESULTS

No patient suffered from hemodynamic instability, serious arrhythmia, or chest pain during or after transesopageal MCE.

Contrast opacification of the left atrial appendage myocardium

Transverse and longitudinal plane views of the left atrial appendage were not imaged in 2 and 4 patients, respectively. One transverse plane view and one longitudinal plane view could not analyzed because of poor image quality. The remaining 96 segments of left atrial appendage myocardium were visually analyzable during MCE. Contrast opacification of the left atrial appendage myocardium was identified in 92 of 96 segments (96%, 95% CI 0.90 − 0.98) by Observer 1 and in 91 of 96 segments (95%, 95% CI 0.88 − 0.98) by Observer 2. The interobserver concordance was 95%. **Fig. 2** illustrates the clear visualization of left atrial appendage myocardial perfusion as a result of intracoronary injection of sonicated albumin. At a constant gain setting, resolution of the left atrial appendage myocardial image is enhanced during MCE, whereas the left atrial appendage cavity remains unopacified. Left atrial appendage myocardial contrast opacification arose strictly from the left, and not from the right coronary artery injection.

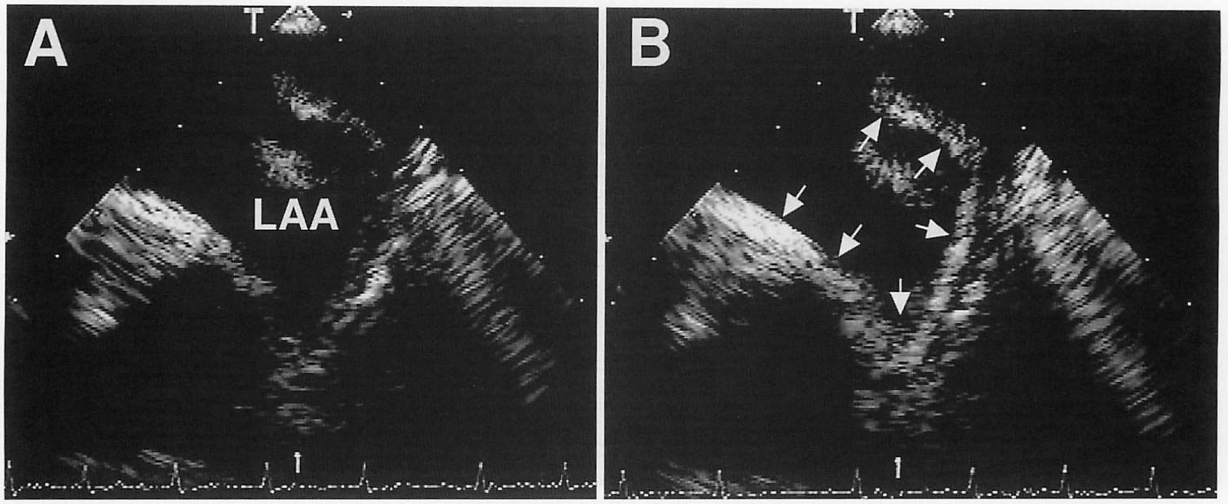

Fig. 2 Transverse plane image of left atrial appendage before (*A*) and during (*B*) intracoronary injection of sonicated albumin in a 62-year-old patient
Perfusion of the left atrial appendage myocardium is distinctly visualized (*B, arrows*).
Abbreviation as in Fig. 1.

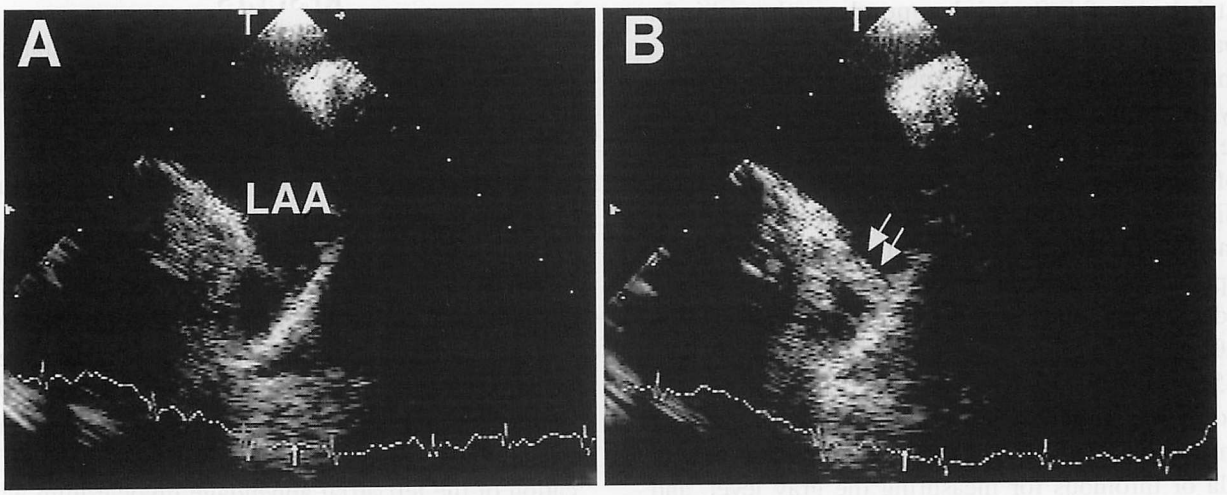

Fig. 3 Transverse plane image of left atrial appendage before (*A*) and during (*B*) intracoronary injection of sonicated albumin in a 74-year-old patient
Contrast opacification of muscular trabeculae (*B, arrows*) is clearly apparent within the left atrial appendage.
Abbreviation as in Fig. 1.

MCE imaging of muscular trabeculae within the left atrial appendage

In 6 of the 16 patients, prominent muscular trabeculae were clearly visible within the left atrial appendage by TEE without contrast. Trabecular muscular perfusion was also successfully imaged by MCE in these patients. In 4 patients, distinct contrast images of muscular trabeculae became apparent that were poorly visualized before MCE. The 2 observers' evaluations of the contrast enhancement of these muscular trabeculae were concordant. **Fig. 3** shows the distinct contrast opacification of muscular trabeculae within the left atrial appendage after the injection of microbubbles. **Fig. 4** illustrates the well-defined muscular trabeculae which were poorly visible before MCE. In 6 patients with prominent muscular trabeculae, the corrected peak videointensity was 0.95 ± 0.15.

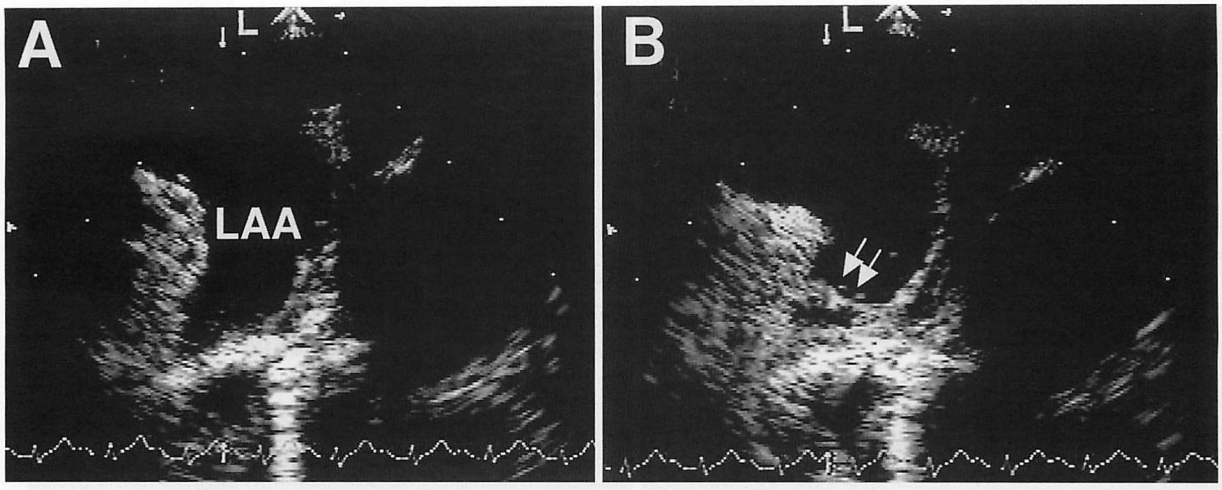

Fig. 4 Longitudinal plane image of left atrial appendage before (*A*) and during (*B*) intracoronary injection of sonicated albumin in a 73-year-old patient
The clearly identifiable muscular trabeculae (*B, arrows*) were poorly visible before the injection of microbubbles. Abbreviation as in Fig. 1.

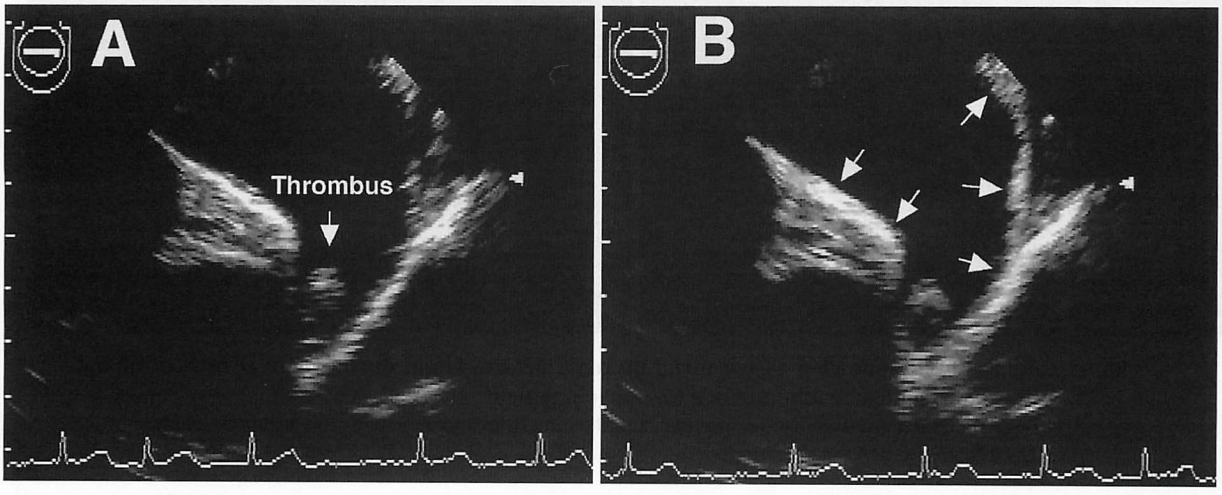

Fig. 5 Transverse plane image of left atrial appendage before (*A*) and during (*B*) intracoronary injection of sonicated albumin in a 49-year-old patient with thrombus contained within the appendage (shown in *A*)
As opposed to the contrast enhancement of the atrial appendage myocardium (*B, arrows*), no contrast opacification enhancement of the thrombus is apparent.

MCE finding of left atrial or left atrial appendage thrombi

In 4 patients with left atrial or left atrial appendage thrombi, neovascularization of the thrombi was not apparent angiographically. Contrast opacification of left atrial or left atrial appendage thrombi was observed visually by neither observer. **Fig. 5** shows no contrast opacification of the left atrial appendage thrombus after the injection of microbubbles. In 4 patients with thrombi, the corrected peak videointensity was 0.15 ± 0.11, significantly lower than that from muscular trabeculae ($p < 0.05$).

MCE finding of left atrial myxoma

In the 3 patients with left atrial myxomas, the tumors originated from the region of the fossa ovalis and were clearly opacified during MCE. Contrast opacification of the myxoma arose from the left coronary injection in only one patient, from the right coronary injection in only one patient, and from either coronary injection in a third patient.

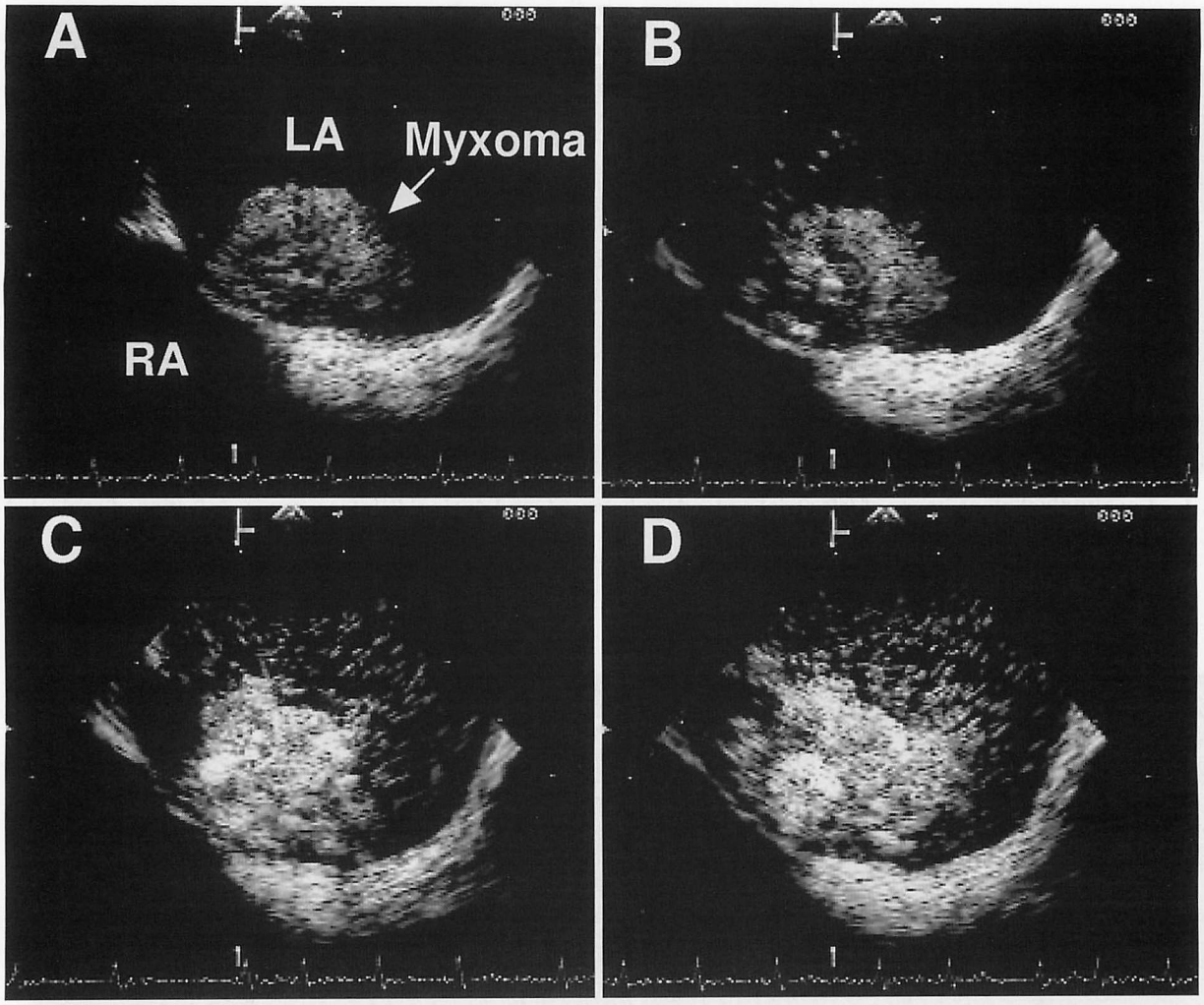

Fig. 6 Longitudinal plane view of left atrial myxoma before (*A*) and during (*B* to *D*) intracoronary injection of sonicated albumin in a 62-year-old patient
Myxoma and left atrial cavity are opacified, and shunting from myxoma to the left atrium is visible.
LA = left atrium; RA = right atrium.

Fig. 6 illustrates the contrast opacification of myxoma, and shunting from the myxoma to the left atrial during MCE.

DISCUSSION

Although left ventricular myocardial contrast effects have been evaluated in a large number of studies[8-11], little is known about the capacity to image the atrial myocardium. Since the atrial myocardium is considerably thinner than the left ventricular myocardium, contrast opacification is difficult, and the potential value of contrast echocardiography in the assessment of atrial myocardial perfusion has not been previously studied. Our study demonstrates the capacity to visualize left atrial appendage myocardial perfusion by transesophageal MCE with intracoronary injection of sonicated albumin microbubbles. In this study, over 90% of left atrial appendage myocardial segments were enhanced by MCE. Attenuation of the left atrial appendage myocardium before MCE, or acoustic shadowing during MCE, were the reasons for absence of contrast opacification. Thus, left atrial appendage myocardial contrast opacification can be expected during MCE in nearly all patients whose left atrial myocardial microcirculation is not compromised. Furthermore, our study also shows that MCE can also offer clear visualization of muscular trabeculae that are barely visible without the injection of microbubbles.

Left heart opacification after intravenous injection of sonicated albumin has been shown to improve the delineation of left ventricular endocardial borders[12]. Likewise, peripheral venous injection of sonicated albumin improves the quality of left atrial appendage echocardiographic images[13]. However, the peripheral venous injection of sonicated albumin combined with fundamental imaging does not provide satisfactory contrast opacification of the atrial or ventricular myocardium. Therefore, this study examined the use of intracoronary injection of sonicated albumin microbubbles to evaluate left atrial appendage myocardial perfusion.

Muscular trabeculations, pectinate muscle and other irregularities are found in the walls of both the left and right atrial appendages. These muscle ridges are small and refractile, usually multiple, and move in concert with the atrial wall. Thrombi are characteristically of a different texture than the atrial wall, are more echo-refractile, uniform in consistency, often pedunculated, and are typically found in the presence of significant atrioventricular valve disease or low cardiac output state. Biplane or multiplane imaging can be helpful in recognizing pathologic conditions of the atrial appendages, and in differentiating them from normal muscle ridges[14], though it may be difficult, even with these techniques, to clearly differentiate a highly trabeculated atrial appendage from a thrombus. In this study, the corrected peak videointensity from thrombi was significantly lower than that from muscular trabeculae, suggesting that transesophageal MCE may be useful to evaluate blood flow into normal structures and abnormal masses within the left atrium.

Microscopic examination shows left atrial myxoma is composed of an acid mucopolysaccharide myxoid matrix in which polygonal cells and occasional blood vessels are embedded[15]. In our observations, all myxomas were clearly opacified by MCE. Thus, it seems possible to differentiate myxoma from fresh thrombus by MCE.

Limitations

Although muscular trabeculae and thrombi were diagnosed according to their characteristic shapes and expected changes of their size or shape over time, this study did not provide histological confirmation. However, since our evaluation focused on typical muscular trabeculae and thrombi, we believe that our results are reliable.

Coronary arteriography in the presence of thrombi may show neovascularization of the region of interest, contrast blush within the thrombi, and fistulous communication with the cardiac chamber to which the thrombi adheres[16]. These angiographic findings most likely represent an advanced stage of evolution of the thrombus. In such cases, it may be difficult to differentiate thrombi from muscular trabeculae by MCE. However, since fresh thrombi without neovascularization tend to be the cause of thromboembolic events, it may be more important to detect them at that early stage.

CONCLUSIONS

We conclude that transesophageal MCE with intracoronary injection of sonicated albumin can image left atrial appendage myocardial perfusion. Our results suggest that MCE allows the evaluation of blood flow into normal structures and abnormal masses within the left atrium. Our MCE findings appear to offer the possibility of differentiating between muscular trabeculations and fresh thrombus. Because of the limited size of our study population, however, this technique requires further evaluation to assess its diagnostic potential fully. MCE may also enable the diagnosis of atrial infarction. With the advent of new contrast media, the evaluation of atrial myocardial opacification by TEE with peripheral intravenous injection of such agents may even become a bedside procedure.

要　約

コントラストエコー図法による左房壁ないし房内構造物の灌流画像化の臨床的意義

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本研究では，超音波攪拌アルブミン冠動脈内注入を用いた経食道心筋コントラストエコー図法により左心耳心筋灌流が可視化できるかを否かを検討した．さらに，左房内の正常構造物(肉柱)および異常構造物(新鮮血栓と粘液腫)への血流も心筋コントラストエコー図法により評価した．

冠動脈閉塞を認めない16症例を対象に，5MHzのバイプレーンもしくはマルチプレーン探触子による経食道心筋コントラストエコー図法を施行した．左心耳心筋を横断面と縦断面それぞれで4分画ずつに分割し，2名の独立した検者が各分画のコントラスト染影の有無を肉眼的に評価した．また，左心耳内の発達した肉柱(6例)と左房・左心耳内血栓(4例)のコントラスト染影も肉眼的に評価した．肉柱または血栓からのバックグラウンドサブトラクション最大ビデオ強度と左心耳心筋からの最大ビデオ強度の比を修正最大ビデオ強度とした．3例の粘液腫のコントラスト染影も肉眼的に評価した．

左心耳心筋の96分画を解析した．検者1では96分画中92分画(96%，95%信頼区間0.90−0.98)で染影が認められ，検者2では96分画中91分画(95%，95%信頼区間0.88−0.98)で染影が認められた．心筋コントラストエコー図法により肉柱は染影されたが，血栓は染影されなかった．血栓の修正最大ビデオ強度は肉柱の最大ビデオ強度と比べ有意に低値だった(0.15±0.11 vs 0.95±0.18，$p<0.05$)．粘液腫は3例とも心筋コントラストエコー図法により良好に染影された．

以上より，超音波攪拌アルブミン冠動脈内注入による経食道心筋コントラストエコー図法は，左心耳心筋灌流を可視化できると考えられた．我々の結果は，心筋コントラストエコー図法により左房内の正常および異常構造物への血流の評価が可能であることを示唆した．

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