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<Original Article>

Usefulness of ultrasound contrast media for cardiac output measurement with echocardiography

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Abstract : The purpose of this study was to determine if contrast media would enhance visualization of the endocardium for assessment of left ventricle (LV) function. In addition, differences between pre- and post-contrast evaluation for the cardiac output measurements including the modified Simpson's method and automated contour tracking (ACT) method were examined. Ten clinically healthy adult beagle dogs (three males and seven females) between 2~3 years old and weighing 6.6~10.8 kg were used. Echocardiographic examinations were performed to compare pre- and post-contrast LV endocardium visualization using a segmental scoring method. Two different methods for measuring cardiac output were also compared. LV visualization was significantly enhanced in post-contrast echocardiography ($p < 0.01$). Significant differences between pre- and post-contrast measurements for the modified Simpson's method ($p < 0.05$) were also observed. No significant difference was found for the ACT method. Contrast echocardiography provides better LV chamber opacification and significantly improves wall segment visualization. Furthermore, contrast echocardiography for measuring cardiac output is helpful for the modified Simpson's method.

Keywords : cardiac output, contrast echocardiography, dog, segmental scoring,

Introduction

Echocardiography has been widely used as a noninvasive diagnostic tool in cardiovascular medicine. It offers a quick, accurate, and inexpensive method to assess cardiac output, the severity of valvular disease, and left ventricle (LV) function [4, 29, 32, 35, 38]. The assessment of cardiac output can provide valuable diagnostic and prognostic information in patients with cardiovascular diseases [25]. The reliable assessment of global and regional left ventricular systolic function is an essential component in evaluating and treating patients with known or suspected heart disease [25]. In addition, echocardiography is a unique technique for providing information about LV wall thickness and contraction, as well as cardiac structure and function, intracardiac masses, pericardial disease, and intracardiac flows and pressures, insufficient tissue perfusion about oxygen, nutrients, and chemical to ensure their survival [3, 15, 25, 31, 33, 34]. Especially, the modified Simpson's method has been routinely used for measurement of left ventricular volume [5, 14, 20, 28]. Also, the automated contour tracking (ACT) methods is a well described methods of evaluating cardiac function due to its reliability and the benefits of its non-invasive technique which have been used for determining cardiac output in humans recently [1, 16, 21, 26, 36].

Despite echocardiography is able to provide high-resolution imaging of LV wall motion, occasionally regional or general endocardial definition is suboptimal, creating the need for methods to improve the depiction of wall motion [8]. Poor visualization of endocardial boders due to suboptimal echocardiographic windows in certain individuals may reduce the value of the test. One approach is to opacify the LV chamber with an echocardiographic contrast agent in order to highlight the endocardial-cavitary interface [6, 7, 13, 17, 18, 22, 23, 24, 37]. The contrast echocardiography has been used to detect the defects in cardiac anatomy and function [10, 11, 19]. to measure cardiac output [9], and to evaluate the repair of cardiac valves [12]. However, a study which compared the difference in detection of LV systolic function before and after contrast enhancement by modified Simpson's method and ACT method has not been reported.

The purpose of this study was to determine if a contrast media would enhance the visualization of the endocardium for the assessment of LV function. Additionally, we tried to evaluate the differences between pre-contrast and post-contrast measurement for the cardiac output measurements including the modified Simpson's method and automated contour tracking method.

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Materials and Methods

Experimental animals

Ten dogs (3 male and 7 female beagle dogs) weighing from 6.6 to 10.8 kg (aged between 2-3 years old) were used for the study and cared for according to the Laboratory Animal Control Guidelines of Gyeongsang National University, which are based on the *Guide for the Care and Use of Laboratory Animals* of the US National Institutes of Health (1996). The animals had free access to drinking water, and were fed once per day and fasted overnight prior to the experiment. Before admission, they were judged to be healthy based upon physical examination, CBC, and serum chemistry. Also all dogs were evaluated by heart worm kit, thoracic radiographs and electrocardiograms.

Instrumentation

The ultrasound machine (Xario SSA-660A; Toshiba Medical Systems, Japan) was used with a 5.0 MHz sector transducer. The echocardiographic studies were performed with the animals in lateral recumbency over a cut-out in the examination table and images and measurements were obtained by scanning from beneath the animals.

Contrast agent

In this study, the second generation contrast agent (SonoVue; Braccco Diagnostics, The Netherlands) was used. The contrast agent was composed of sulfur hexafluoride-filled microbubbles. After routine echocardiography was performed, 0.5 mL of the contrast agent was injected via an IV line followed immediately by 5 mL of normal saline solution flush [27].

Measurement of segmental scoring

Endocardial segments were assigned based on previously established methodology [7, 13], whereby the four-chamber views of the LV were divided into 6 segments. This method offered a simpler and more practical approach than the more complex 16-segment model used by the American Society of Echocardiography [7, 13] (Fig. 1). A score of 1 was assigned to a wall segment if it was visualized in both systole and diastole. A score of 0 was assigned to the segment if it was not visualized. At the end of each echocardiographic study, the segmental scores were expressed by the total summation of the scores of each 6 segments.

Modified Simpson's method

The left ventricular long axis is specified by tracing the left ventricular endocardium on the apical long-axis cross-sectional images (four-chamber cross-sectional images) acquired in two dimensional echocardiographies. The left ventricular volume was calculated as the sum of the volumes of 20 elliptic disks perpendicular to the left ventricular long axis. The endocardial surfaces of the apical four chamber echocardiographic images were recorded at end-diastole and end systole. The end-diastolic frame was specified as the frame coinciding with the beginning of the Q-wave or just before the mitral valves closed. An end-systolic frame was identified as the frame near the end of the T-wave or just before the mitral valve opened. The values presented have been taken as the mean of three cardiac cycles in breath-held expiration after contrast injection was performed same steps were repeated (Fig. 2A and B).

ACT method

To perform ACT measurement, the optional USAT-770A (Xario SSA-660A; Toshiba Medical Systems) was used. The ACT measurement was performed as offline analysis from two-dimensional echocardiographic single display and cine frame-advance playback mode. For this measurement, it was necessary to display a long-axis cross sectional image from the cardiac apex (apical four chamber view). If the frame rate is low, the end-diastolic and end-systolic images may not be acquired within the start and end of the measurements. So, it was performed that the frame rate was set to be 30 fps (frames/sec).

In each case, the end-diastolic images by left apical four chamber view were displayed. The end-diastolic images were defined as the visually estimated largest cavity area. In this image, an operator appointed three points where cardiac apex on the endocardium and very bright areas that were at the

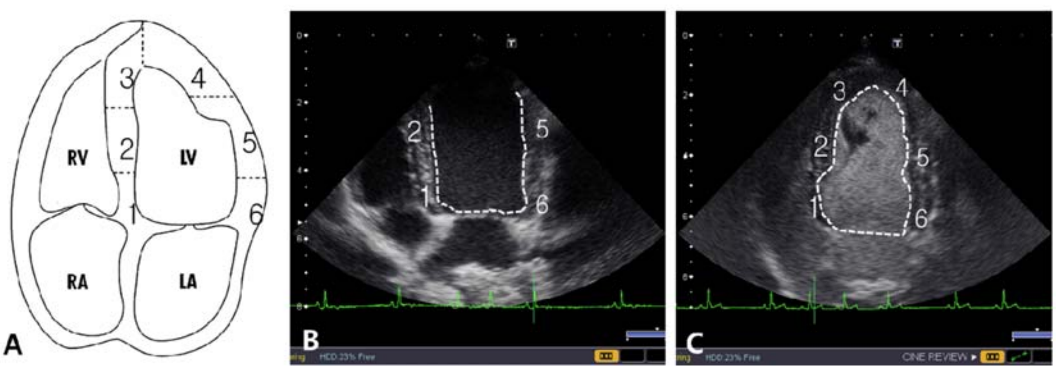

Fig. 1. Four-chamber view of LV divided into 6 segments in dogs. Schematic drawing (A), pre-contrast (B), and post-contrast (C) echocardiographic images for segmental scoring. RV: right ventricle, LV: left ventricle, RA: right atrium, LA: left atrium.

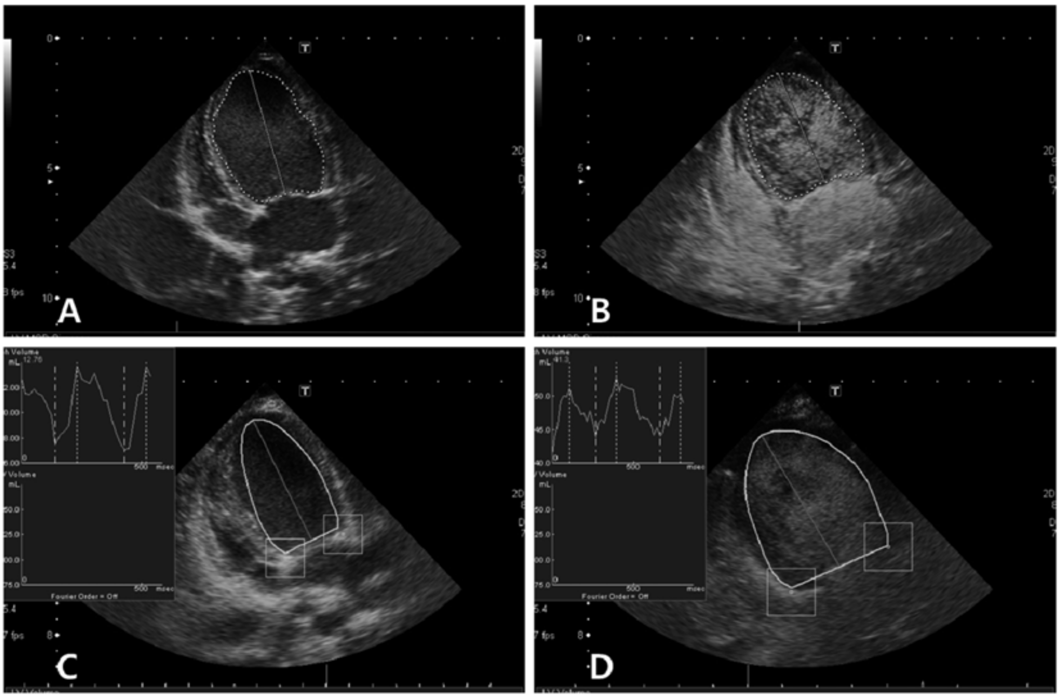

Fig. 2. Pre-contrast and post-contrast echocardiographic images of left ventricle by the modified Simpson's method and automated contour tracking (ACT) method. (A) Pre-contrast images by the modified Simpson's method. (B) Post-contrast images by the modified Simpson's method. (C) Pre-contrast images by the ACT method. (D) Post-contrast images by the ACT method.

junction of the cardiac muscle and the valve ring. After three locations were appointed, the tracking contour was performed automatically with the trace line connecting three locations. The tracking of the endocardial border of the left ventricular cavity was completed after tracking the last image of the number of two cardiac cycles. In ACT measurement, the frame range to be measured was calculated from the heart rate. Each case's heart rate was obtained from the ECG. After contrast agent injection was performed same steps were repeated (Fig. 2C and D).

Data analysis

Statistical analysis was performed with SPSS version 14.0. A paired sample *t*-test was used for statistical difference between the pre-contrast and contrast studies groups. For all tests, p values < 0.05 were considered significant.

Results

Left ventricle visualization by the segmental scoring

The contrast enhancement was evaluated the visualization of left ventricle by the segmental scoring. The baseline echocardiograms in 10 beagle dogs had an average segmental score of 3.80 ± 0.63 (mean ± SD, range 3 to 5). After contrast injection, the average segmental score was increased to 5.20 ± 0.79 (mean ± SD, range 4 to 6; Fig. 3). There was a significant enhanced visualization of the LV in post-contrast echocardiography (p value = 0.007).

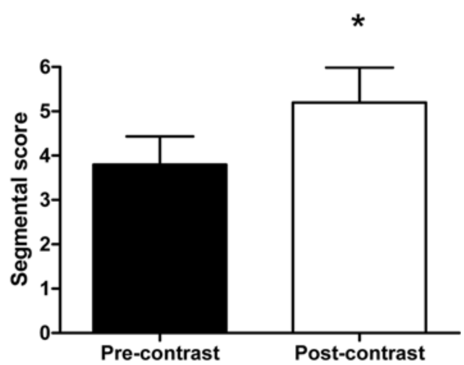

Fig. 3. Comparison of left ventricular visualization by scoring method between pre-contrast and post-contrast. Asterisk (*) indicates significant difference ($p < 0.05$).

Comparison of pre and post cardiac output by the modified Simpson's method and ACT method

Cardiac output measurements by the modified Simpson's method and ACT method were performed in 10 beagle dogs. The pre-contrast results ranged from 0.621 to 1.656 L/min (mean ± SD, 1.195 ± 0.335 L/min) and 0.305 to 1.774 L/min (mean ± SD, 1.307 ± 0.982 L/min). On the other hand, post-contrast results range from 0.459 to 1.461 L/min (mean ± SD, 1.022 ± 0.335 L/min) and 0.327 to 1.394 L/min (mean ± SD, 0.882 ± 0.352 L/min) for the modified Simpson's method and the ACT method respectively (Table 1).

Table 1. Volumetric evaluation of cardiac output by two echocardiographic measurement methods with pre-contrast and post-contrast in beagle dogs (n = 10)

Methods	Pre-contrast cardiac output (L/min)	Post-contrast cardiac output (L/min)	*P* value
The modified Simpson's method	1.195 ± 0.335	1.022 ± 0.335	$p = 0.011$
The ACT method	0.982 ± 0.407	0.882 ± 0.352	$p = 0.333$

All data represent mean ± SD.

Discussion

Although echocardiography can be considered as an excellent tool to assess LV function, regional wall motion and valvular diseases, it has limited usefulness in case of poor echocardiographic images [25]. The LV function and regional wall motion assessment are important factor in managing patients [34]. Patients tend to have more difficult echocardiographic images for a variety of reasons including mechanical ventilation and inability of appropriate positioning for the echocardiograhic study. With the use of contrast agents, patients with poor echocardiographic images, which can be considered as nondiagnostic studies, can be converted to diagnostic studies yielding more accurate data. The increased signal-to-noise ratio detection by harmonic imaging will result in an increase in the video intensity, resulting in a greater success rate of LV opacification after an injection of contrast agent [6, 7, 13]. The use of myocardial contrast echocardiography results in improved diagnostic accuracy and cost effectiveness. In this study, we found significant improvement in LV wall visualization at the post-contrast scoring method. However, the complete visualization of each segment was not common in post-contrast study. The reason may be attributable to differences in characteristics of species between human and dog due to faster heartbeat.

In this study, the contrast agent did not completely fill the left section 3 and 4 of left ventricular cavity. As such, the area is difficult to evaluate. It seems that there has been whirling motion of contrast agent as it bounced back after striking the wall of left endocardium. Therefore, in order to solve the problems, depending on the nature of the testing species such as their body weight, further studies in figuring out the correct volume of contrast agent should be pursued.

In the modified Simpson's method, pre-contrast cardiac output was 1195.3 mL/min, and post-contrast cardiac output was 1022.3 mL/min. This result may suggest that cardiac output measurement without the injection of contrast agent seems to yield more exaggerated measurement in the LV endothelium. Therefore, the use of contrast agent is useful in the modified Simpson's method to yield more accurate evaluation. There was no significant difference in cardiac output when measured with ACT method. In ACT method, it seems that there has not been a significant contribution of contrast agent in terms of effectiveness in measuring cardiac output in dogs. Such phenomenon may be attributable to the absence of rather biased region of interest when measuring LV endocardium by human eyes.

The advantages of sulfur hexafluoride-filled microbubbles are the prolonged stability up to 6 h in the vial, relatively prolong half-life of 6 min in the peripheral blood, and the uniformity of their size, which improves backscattering and harmonic behavior at low acoustic power [2, 30]. In this study, we used the contrast agent composed of sulfur hexafluoride-filled microbubbles. This contrast agent provides a nonlinear response with production of a clinically useful signal at low acoustic pressures and limited destruction of the microbubbles.

Mechanical Index (MI) was used as an important factor in terms of measuring accurate amount of initially administered contrast agent because of destruction of microbubbles as MI increase may cause increased acoustic pressure [2, 30]. In this study, MI values were constant as 0.7 for controlled condition. Further studies should be conducted in measuring cardiac output by using contrast agent along with varied MI.

In conclusion, contrast echocardiography provides better LV wall visualization. Using contrast echocardiography to measure the cardiac output is helpful in modified Simpson's method. Additionally, it may be useful to diagnose cardiac diseases such as intracardiac shunting disorder.

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