Proceedings of the 28th IEEE
EMBS Annual International Conference
New York City, USA, Aug 30-Sept 3, 2006

Ultrasonic Doppler Vibrometry: Measurement of Left Ventricular Wall Vibrations Associated With Coronary Artery Disease

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Abstract— **We have developed a new method of detecting coronary artery stenoses that uses Doppler ultrasound to measure minute local vibrations in the cardiac wall associated with post-stenotic flow turbulence. In this paper, we present the results of a preliminary clinical study to evaluate the efficacy of this method for detecting coronary artery disease (CAD) using coronary angiography as the gold standard. The study population consisted of 34 patients clinically-indicated for coronary angiography. Based on the catheterization reports, the patients were divided into three categories: *severe* (obstructive CAD, typically with >70% diameter reduction), *moderate* (non-obstructive CAD, typically with <50% diameter reduction or diffuse atherosclerosis), and *normal* (no angiographic evidence of CAD). A diastolic myocardial vibration index (DMVI) was calculated as the ratio of the normalized periodogram spectral energy in the 100~800-Hz frequency band of the instantaneous wall velocity in early diastole to a baseline value during diastasis. The DMVI was significantly higher in *severe* CAD patients (21.2±3.2 dB) compared to *moderate* CAD (17.5±3.5 dB) and *normal* (11.2±4.8 dB). The differences between each of the categories were statistically significant ($p<0.05$). *Severe* CAD patients could be distinguished from *normal* with a sensitivity of 91.7% and specificity of 83.3%. We believe that this method could potentially be developed into a low-cost and accurate test for diagnosis and screening for coronary artery stenosis.**

I. Introduction

Coronary artery disease (CAD) accounts for 495,000 deaths and costs $142 billion annually in the US [1].

The primary cause of CAD is coronary artery stenosis, which is the partial or complete blockage of one or more coronary arteries due to buildup of atherosclerotic plaque.

Symptoms of CAD often appear at an advanced stage of the disease, making early detection and prevention especially challenging. According to the American Heart Association, 50% of men and 64% of women who died suddenly of CAD had no previous symptoms of this disease [1]. The primary prevention strategy for CAD is based on risk factor screening and risk reduction [2]. Evidence indicates that risk assessment using the traditional risk factors, such as age, smoking status, cholesterol levels and hypertension, leads to a substantial detection gap, particularly in asymptomatic individuals [3]. Early detection of CAD has the potential to enable more effective primary prevention of myocardial infarction and death and lower healthcare costs by avoiding costly hospitalizations and expensive interventions. Screening for CAD remains controversial primarily because existing diagnostic tests either have insufficient accuracy or are prohibitively expensive [4].

We have developed a new ultrasonic method for detecting coronary artery stenoses based on the measurement of minute vibrations of the left-ventricular (LV) wall produced by post-stenotic flow turbulence [5]. In peripheral arteries, the flow distal to a stenosis develops eddies even in cases of mild stenosis. Vascular sounds called bruits or murmurs are produced when these eddies strike the vessel wall producing vibrations at an audible frequency. The frequency is inversely proportional to the residual lumen diameter of the stenosis [6]. Coronary artery stenoses have also been associated with murmurs produced by flow turbulence distal to the stenosis. These high-pitched diastolic murmurs have been observed in several case reports [7][8]. However, the weak intensity and sharp localization prevents the detection of these murmurs by auscultation with a stethoscope through the chest wall in the majority of cases. Our approach uses Doppler ultrasound to directly interrogate the vibrations at their point of maximal intensity on the left-ventricular epicardial wall, thus providing a significantly improved sensitivity for detection of weak vibrations.

Tissue vibrations appear as a characteristic pattern of harmonic bands in pulsed Doppler spectral waveforms [5]. Clutter filters in conventional Doppler systems typically suppress these motions to highlight the blood flow, whereas Tissue Doppler systems highlight the mean tissue velocity signals. Thus, vibrations have received limited attention in conventional ultrasound exams. We have developed an ultrasonic Doppler vibrometry technique for quantitatively measuring tissue vibrations from ultrasonic echo signals, [5]. We have developed a prototype vibrometry system based on a software-

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programmable ultrasound system [5][9]. In this paper, we report the results of a preliminary clinical study to evaluate the feasibility of our approach. The objective of this study is to evaluate the correlation between an index based on the measurement of LV wall vibrations and angiographically-diagnosed CAD.

II. Methods and Materials

34 patients (13 women) clinically-indicated for left-heart cardiac catheterization were recruited for an ultrasound examination following an informed consent procedure approved by the University of Washington Human Subjects Review Committee. The recruited patients underwent coronary angiography at the University of Washington Medical Center.

The ultrasound examination was performed prior to catheterization. The LV wall segments perfused by the three major coronary arteries were interrogated using pulsed-wave (PW) Doppler ultrasound. The quadrature-demodulated Doppler ultrasound data prior to conventional Doppler signal processing were acquired from a 15-mm range gate using the HiVision 5500 ultrasound system (Hitachi Medical Systems America, Twinsburg, OH) [9]. The quadrature-demodulated Doppler data were processed using autocorrelation to estimate a time series of instantaneous wall velocities in the time intervals between successive pulse transmissions (Fig. 1(a)).

To analyze the frequencies contained in the LV wall motion, a waveform of the periodogram power spectral density estimate of the instantaneous velocity was computed (Fig. 1(b)). The periodogram power spectral waveform shows the change in the relative power in various vibration frequencies present in the wall velocity at different time points in the cardiac cycle. It is different from the conventional Doppler spectral waveform, which shows the mean velocity of the wall motion. Vibrations produce increased power in high frequency bands in the periodogram power spectral waveform (Fig. 1(b)). To obtain a quantitative measure of diastolic vibrations, the spectral energy in the 100~800 Hz frequency band was computed. The spectral energy was normalized by the energy in the 800~1000 Hz frequency band to compensate for differences in noise power. A diastolic myocardial vibration index (DMVI) was calculated as the ratio of the median peak value of vibration energy in early diastole (typically, immediately after isovolumetric relaxation) to a baseline value during mid diastole or diastasis (Fig. 1(c)). The result was expressed on a logarithmic scale (dB). If significant spectral energy was present during mid-diastole or diastasis, the baseline value was determined during late systole, as shown in Fig. 1(f). The instantaneous myocardial velocity waveform was used as a guide to determine the onset of diastole.

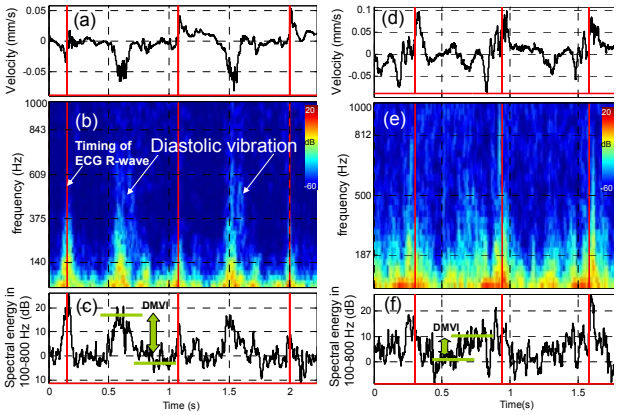

Figure 1. (a) Wall velocity of anterior LV in a patient with obstructive multi-vessel CAD. (b) Periodogram of wall velocity. (c) Normalized spectral energy between 100~800 Hz. The measurement of DMVI is indicated using the green arrow. (d), (e) and (f) Corresponding graphs for a angiographically-normal subject.

Based on the cardiac catheterization reports, patients were divided into three disease groups: (1) *severe* CAD (obstructive CAD, typically with >70% diameter reduction or a fractional flow reserve of <0.75); (2) *moderate* CAD (non-obstructive CAD, typically with <50% diameter reduction or diffuse atherosclerosis) and (3) *normal* (no angiographic evidence of CAD). Patients with severe valve disease were excluded from the data analysis.

III. Results

Patients with *severe* CAD were somewhat older (67±14 years (mean ± standard deviation)) compared to patients with *moderate* CAD (61±13 years) and *normal* (54±10 years). The DMVI (Fig. 2) was significantly higher in *severe* CAD patients (21.2±3.2 dB) compared to *moderate* CAD (17.5±3.5 dB) and *normal* (11.2±4.8 dB). The differences between each of the categories were statistically significant ($p<0.05$).

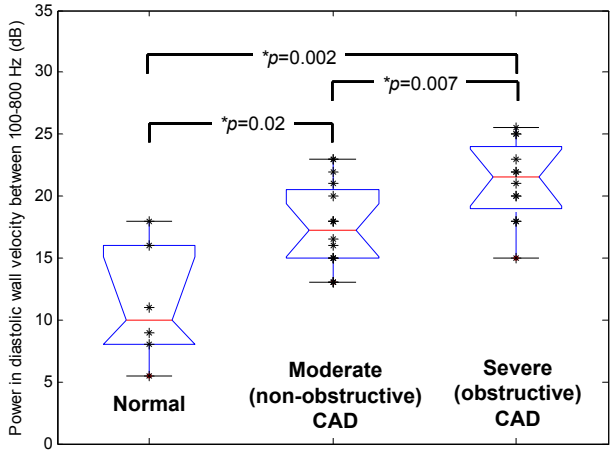

Figure 2. Differentiation between CAD severity using DMVI.

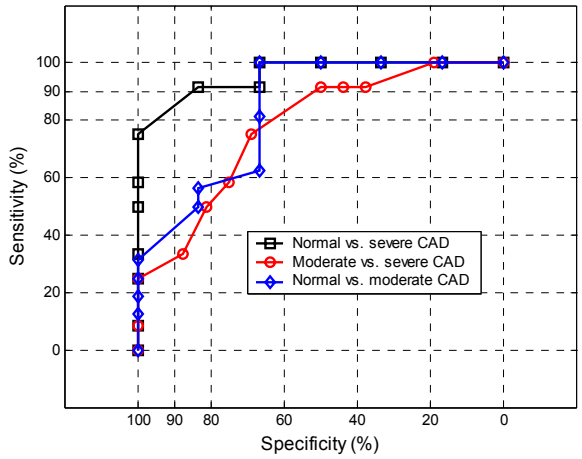

Figure 3. ROC curves for classifying CAD severity.

Figure 3 shows the receiver operating characteristic (ROC) curves for differentiating between the three groups (*severe*, *moderate* and *normal*). *Severe* CAD patients could be distinguished from *normals* with a sensitivity of 91.7% and a specificity of 83.3%. In addition, *severe* CAD patients could be distinguished from *moderate* CAD with a sensitivity of 75% and a specificity of 68%.

IV. DISCUSSION

Several reports have described the presence of a high-pitched diastolic murmur in patients with coronary artery stenoses [7][8]. The cause of the murmur has been hypothesized to be coronary flow turbulence distal to the stenosis. Although the high-pitched diastolic murmur is a unique finding associated with coronary artery stenosis and provides a direct marker for the presence of obstructive coronary disease, it is not commonly detected via auscultation. It has been hypothesized [8] that this flow murmur is in fact present even in stenoses with only 25% diameter reduction; however, the weak intensity and sharp localization prevents detection by auscultation. Several researchers have proposed signal processing methods to improve the detectability of diastolic coronary murmurs [10][11]. Although the results were promising, these acoustic markers of CAD have been overlooked in favor of modern imaging-based diagnostic tests due to the limited sensitivity of auscultation and phonocardiography.

PW Doppler ultrasound is capable of detecting displacement with very high resolution, e.g., 40 nm, because the time of flight of a received ultrasound echo can be measured very accurately using analog-to-digital converters that operate at a high sampling frequency, e.g., 40 MHz, with high dynamic range, e.g., 12 bits or more. In addition, PW Doppler can interrogate vibrations transcutaneously at their source of maximal intensity. Therefore, PW Doppler vibrometry is capable of significantly improving the sensitivity compared to auscultation and phonocardiographic methods. Quantitative indices of the estimated vibration characteristics, such as DMVI, can therefore be used as an accurate test for the presence of CAD.

The presence of diastolic vibrations, as evidenced from high frequency content in the periodogram and the presence of double-sided harmonic bands in the Doppler spectral waveform, is not by itself a specific indicator of CAD. Since the DMVI is normalized by a baseline value, typically during diastasis, it may be used to discriminate between vibrations based on their timing and intensity in the cardiac cycle. In our study population, diastolic vibrations were observed of 3 out of 6 angiographically-normal subjects. In one patient (36-yr old, female), the vibrations were present both in systole and throughout diastole, thus yielding a low value of DMVI. This diabetic patient was undergoing cardiac catheterization in preparation for a kidney transplant and was found to have mild mitral annular calcifications and mildly elevated LV end-diastolic pressure (20 mmHg). The vibrations were most prominent near the papillary muscle. The second patient (59-yr old, male) had a history of diabetes, hypertension and metabolic syndrome. Angiography revealed small coronary vessels with moderate tortuosity with no evidence of atherosclerosis. The vibration intensity was low compared to baseline, yielding a low value of DMVI. The third patient (62-yr old, male) was undergoing catheterization as routine follow-up after cardiac transplantation. Angiography revealed a tortuous aorta with no significant coronary artery disease. Low-intensity vibrations were observed. It is likely that the vibrations were caused in these patients by the above mentioned confounding factors. Further studies analyzing the cause of diastolic vibrations in normal patients (other than vibrations due to valve disease) need to be performed.

The characteristic signature of narrowband vibrations in the Doppler spectral waveform consists of double-sided harmonic bands. In some patients with angiographic evidence of *moderate* or *severe* CAD, such a characteristic signal was not apparent, although a high value of DMVI was observed. In these patients, it is likely that the vibrations were broadband, causing an increased variance of the Doppler spectral waveform thus masking the characteristic harmonic signature.

The most probable cause of the observed diastolic vibrations is post-stenotic flow turbulence in the coronary arteries. However, vibrations could also be caused by the sudden deceleration of blood during early filling due to reduced diastolic compliance. The relationship of the observed vibrations with the third and fourth heart sounds associated with CAD needs to be further elucidated [12]. All patients in our current study population were clinically-indicated for cardiac catheterization, predominantly due to suspected CAD. Additional studies using asymptomatic patient populations are needed to investigate the effect of confounding factors, such as diastolic dysfunction, on the observed index of vibration.

Emerging technologies for the diagnosis of CAD, such as 64-slice computed tomography (CT) and magnetic

resonance angiography are associated with high costs [3][13][14][15]. Exercise ECG has been suggested as a screening test for CAD owing to its low cost. However, it has poor positive predictive value in populations with a low risk of CAD, and poor negative predictive value in high-risk populations [13]. Coronary artery calcium scores may be more appropriate for early-stage detection but have been controversial due to low specificity [3]. Among the existing noninvasive imaging modalities, nuclear stress test is the most accurate, with sensitivity of 85-87% and specificity of 64-85% [13]. Other emerging methods, such as brachial artery reactivity testing for endothelial function have shown promise in preliminary studies but are limited by high biologic variability [4].

Our preliminary study indicates that Doppler vibrometry can be used to differentiate normal patients from those with obstructive CAD with high sensitivity and specificity matching that of nuclear stress tests. With further refinement of the ultrasonic scanning and data acquisition protocol, we believe that the sensitivity and specificity can be further improved. In addition to being noninvasive and safe, a screening test based on Doppler vibrometry will have the advantage of directly assessing coronary obstructions and can potentially be administered using a simple low-cost instrument in a primary care setting.

V. CONCLUSION

Preliminary evidence indicates that the measurement of left ventricular wall vibrations using Doppler ultrasound could lead to a new low-cost and accurate method for early non-invasive diagnosis and screening of coronary artery disease. Flow turbulence distal to a coronary artery stenosis is the most likely cause of the localized wall vibrations. Additional studies investigating the mechanisms producing wall vibrations in coronary artery disease are warranted.

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