THE INVESTIGATION OF THE RELATIONSHIP BETWEEN CAROTID INTIMA-MEDIA THICKNESS AND VASCULAR COMPLIANCE IN PATIENTS WITH CORONARY ARTERY DISEASE

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ABSTRACT

Carotid artery intima-media thickness (IMT) is used as an indicator of atherosclerosis and a risk predictor for stroke and cardiovascular diseases. In macroscopic view, the atherosclerotic process constitutes changes in structure and mechanical function of vessels. The aim of this study was to investigate the relationship between carotid IMT and elastic property, or compliance, of the vessel.

Eighteen patients (10 males, 8 females, mean age: 65.5+/-12.2) who received coronary angiography due to coronary artery disease (CAD) were enrolled in this study. The IMT was measured at left carotid artery 5 cm below bifurcation. The blood pressure was measured through a catheter placed in aortic arch and continuous pressure change was recorded simultaneously during performing of carotid sonography. A sequence of cross section images of carotid sonogram was recorded. An image analysis algorithm is developed for serial luminal area measurements. Then the estimation of compliance was computed according to Windkessel model.

Regression analysis shows negative correlation ($r=-0.704$) between IMT and vascular compliance. The results correlate the elastic property and structural change of carotid artery during the process of atherosclerosis. This finding further support that IMT is a good parameter for evaluation of the severity of atherosclerosis..

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1. INTRODUCTION

Carotid intima-media thickness (IMT) was used as an indicator of atherosclerosis [1-2]. It provides a non-invasive method for risk assessment of stroke and

cardiovascular disease [3-5]. In macroscopic view, the atherosclerotic process constitutes structural and functional changes of a vessel. The IMT is a measurement for vascular structural changes. To evaluate the vascular function, there are a lot of approaches proposed to quantify the mechanical properties of vessels, such as compliance.

In this study, windkessel model was used to measure the compliance of carotid artery. Windkessel model, which was first introduced by Otto Frank in 1899 [6] and has been modified into several sophisticated forms thereafter [7-9], is frequently used to describe the load faced by the heart in pumping

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blood through the arterial system. The simplest classic two-element Windkessel model was used in this study. In this model the circulation is viewed in terms of parallel capacitance and resistance components. The resistance term corresponds with peripheral vascular resistance and essentially, together with cardiac output, determines the level of mean arterial pressure. The capacitance element corresponds with arterial compliance, which is predominantly contained within the aorta and contributes to the phasic properties of the circulation, usually determined as pulse pressure. The corresponding electric circuit is illustrated as figure 1. According to Kirchhoff's Law, we can obtain the differential equation:

$$C \frac{dp(t)}{dt} + \frac{P(t)}{R} = I_1(t) \quad (1)$$

During diastole, when there is no blood flow from the heart, $I_1(t) = 0$, and thus the equation can be solved as:

$$P(t) = P(0) e^{-\frac{t}{RC}} \quad (2)$$

The $P(0)$ is the pressure at aortic valve closure. Let τ be the time constant of the pressure decay curve, the compliance can be obtained, $C = \tau / R$. This means that arterial compliance can be determined from the pressure half time of the diastolic pressure decay curve.

2. MATERIAL AND METHODS

Eighteen patients (10 males, 8 females, mean age: 65.5 ± 12.2) of CAD who received coronary angiography in department of internal cardiology of National Cheng Kung University Hospital were recruited in this study. Before performing of angiography, we placed the catheter in the aortic arch.

Fig. 1. Two-element Windkessel model

Continuous blood pressure was recorded and B-mode sonography of carotid artery was obtained simultaneously. All the images of carotid artery were obtained from the HP 5500 system with a 7.5 MHz probe. Left common carotid artery was measured in all patients because it was bifurcated directly from aortic arch and thus its pressure changes may be more close to that of aortic arch. Longitudinal section was obtained first for the measurements of IMT, which was measured in the common carotid artery at 5 cm below carotid bifurcation. Cross-sectional images were then recorded at this area for 3 to 4 cardiac cycles. All the images were recorded by a tape and then digitalized by an image grabber card (UPMOST 403A) with the rate of 15 frames /sec. The data was then stored as a sequence of 640*480 BMP files for further processing and analysis.

The IMT can be measured directly from HP 5500 system by marking the luminal edge and the boundary between external elastic membrane and adventitial layer manually. The distance between these two marks was IMT and it could be measured by the built-in function of HP 5500.

The ultrasound images were processed by program developed on the Matlab 5.3. It needs a lot of pre-processing on ultrasound images because the noise and limitations of ultrasound images. Thus the images were pre-processed by compression of dynamic range to enhance most parts of low gray-level in ultrasonic images [10]. In addition, median filter was used to suppress speckle in these images [11]. Then a semi-automatic edge-detection program was applied to the pre-processed images to determine the luminal edge and thus got the area of vascular lumen in each cardiac phase. The semi-automatic edge-detection program worked as following: (1) The pre-processed image was loaded and a square ROI of 200x200 pixels was selected with the cross-section of a vessel included. (2) A reference line in radial direction would show by the program every 24° . The approximate point of luminal edge in the radial direction has to be pointed manually (thus fifteen points would be marked for each circle of lumen). These points were used only as a basis for following step of auto-detection. Therefore, even the points were marked with some errors and the edge can still be determined. (3) Another four points were interpolated on the radius between each two manually marked points. Then these points were used as the initial points on the algorithm to search the luminal edge along the radial direction as shown in figure 2. (4) The algorithm of the edge-detection program was based on the 1st degree of derivative. Maximal point of 1st degree derivative was considered as the edge [10]. (5) The circle of luminal edge was obtained by connecting each edge points searched by the program. To avoid a zigzag boundary, a smooth operator was

applied to yield a smooth luminal circle. The smooth operator was described as following:

$$S = \frac{[11111]}{5}; X' = \text{conO}(S, X); Y' = \text{conO}(S, Y) \quad (3)$$

Since the luminal edge of serial cross-sectional images was obtained from above method, a sequential luminal area in a cardiac cycle can be obtained. In addition, the signal of pressure change detected by a catheter was introduced to the HP 5500 system via com port and the pressure wave was shown on the screen. The cursor on pressure curve indicated the time point at which the image was obtained as shown in figure 3. Thus we can get the corresponding pressure change information. The averaged pressure in diastolic phase divided by an average of corresponding luminal areas was used as an indicator of vascular resistance (R). Then the compliance was computed according to equation 2.

3. RESULTS

An example of luminal boundary determined by the program is shown in figure 4. A sequence of luminal area in a cardiac cycle is shown in figure 5. The computed compliances of 18 patients are shown in Table I. Correlating the compliance with IMT by regression analysis to get the correlation coefficient (-0.704) as shown in figure 6. This result implies that increased IMT may indicate decreased vascular compliance.

Fig. 2. The stars are the points marked manually according to the reference lines ($r_1, r_2, \dots$) which are given every 24° (θ). Another four points are interpolated on the radius between each two manually marked points. Then these points together will be used as the initial points for the program to search the luminal edge along the radial direction.

Fig. 3. The cursor (arrow) on pressure curve indicates the time point at which the image was obtained.

Fig. 4. An example (patient 11) of luminal boundary determined by image-processing programs.

Fig. 5. An example of serial lumen areas on a cardiac cycle (patient 5).

Table I : vascular average area; P : average blood pressure; R : peripheral resistance; τ : pressure decay time constant; C : compliance; IMT : intima-media thickness

patient	A (mm^2)	P (mmHg)	R ($\frac{\text{mmHg}}{\text{mm}^2}$)	τ	C ($\frac{\text{mm}^2}{\text{mmHg}}$)	IMT (mm)
1	79.23	82.99 ± 20.95	1.05	0.65	0.62	1.81
2*	70.21	96.64 ± 28.79	1.38	0.80	0.58	2.25
3	70.49	106.99 ± 21.58	1.52	1.72	1.13	0.33
4	72.73	107.34 ± 22.19	1.48	1.38	0.93	0.66
5	62.04	108.25 ± 13.03	1.74	2.18	1.25	0.75
6	56.39	121.49 ± 28.73	2.15	0.82	0.38	1.36
7	74.54	106.02 ± 18.97	1.42	1.92	1.35	0.75
8	64.46	114.10 ± 18.54	1.77	1.96	1.11	0.15
9	68.92	75.94 ± 10.36	1.10	1.95	1.77	0.15
10	78.77	108.08 ± 28.17	1.37	0.90	0.66	1.28
11	74.51	92.59 ± 23.38	1.24	1.60	1.29	0.82
12	79.83	94.03 ± 25.46	1.18	1.53	1.30	0.82
13	66.87	126.53 ± 19.01	1.89	3.12	1.65	0.64
14*	64.72	125.74 ± 25.00	1.94	1.40	0.72	2.15
15*	70.50	98.76 ± 22.17	1.40	0.50	0.36	1.56
16*	80.71	91.43 ± 21.91	1.13	0.96	0.85	1.28
17	49.29	133.82 ± 36.75	2.72	0.98	0.36	1.01
18	44.61	83.34 ± 24.30	1.87	1.40	0.75	1.19

Fig. 6. The relationship between IMT and vascular compliance ($r = -0.704$).

4. DISCUSSION

Many methods were proposed to estimate the mechanical properties, such as compliance, of regional or systemic vessels [12-13]. Some sophisticated methods, though getting a better estimation, can only be calculated in vitro. On the other hand, although arterial compliance may be estimated non-invasively by some approaches, most currently available techniques have their shortcomings, including the inability to allow for the impact of arterial distending pressure and structural adaptation [14]. Because cardiovascular system is adapted by a complicated physiological mechanism, and the mechanical property of vessels must be changed dynamically, it is no doubt that the system is a non-linear system. It is not surprising that the property measured in different

methods may result in different results. The Windkessel model provides a simple way to estimate the vascular compliance in vivo with the consideration of the role of each component in different cardiac phase, and can be calculated by curves of pressure and volume change. The data can be obtained with popular facilities in cardiovascular department in most hospitals. Though the catheterization process is invasive, these patients have to receive this procedure for the necessity of their diseases, and little additional risk was added to them.

To avoid the inter-observer and intra-observer variability, computerized image processing was used in determining the luminal boundary in sonograms. The searching results for an experienced cardiologist are used to check the validity of the results obtaining the algorithm. The program-searched 90 points (every 4°) on the circle were correlated with those points on manually traced boundary in corresponding radial direction. The point-to-point correlation coefficient was 0.976 as shown in figure 7. In addition, to test the reproducibility of this program, the results from different beginning points for searching were compared. The same sonogram was marked for the beginning points of searching in 24 different times. The computed luminal areas were collected for statistical analysis. The reproducibility was 0.979 as shown in figure 8.

Carotid ultrasonography is a non-invasive and convenient tool and has been widely used in evaluation of patients with cerebral vascular diseases. The IMT can be easily obtained by carotid ultrasonography and is an important parameter in this examination because the value of IMT in prediction of the degrees of atherosclerosis and the risk of stroke and cardiovascular disease has been demonstrated by a lot of studies [3-5]. In addition, arterial compliance is the most important determinant of hemodynamics, and therefore, may be the root cause of a host of cardiovascular complications and events [12-13]. Some studies have demonstrated the relationship between carotid IMT and mechanical property of carotid wall in hypertensive patients. [15-16]. However, to our knowledge, there have been few studies dealing with the relationship between IMT and vascular compliance in patients with cardiovascular diseases. This study correlated the changes of structure and mechanical properties of vessels in patients with CAD. According to these results, larger carotid IMT is associated with lower values of vascular compliance. This finding suggests that IMT is not only a parameter of structural changes of vessels but also provides an indicator for mechanical property, and thus it is good for evaluation of the severity of atherosclerosis.

Fig. 7. The point-to-point correlation coefficient between manually marked boundary and computer processing ($r = 0.976$).

Fig. 8. The same sonogram was marked for the beginning points for searching in 24 different times.

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