Ultrasound in Med. & Biol., Vol. 40, No. 3, pp. 611–621, 2014

0301-5629/$ - see front matter

http://dx.doi.org/10.1016/j.ultrasmedbio.2013.10.008

● *Original Contribution*

USE OF WAVE INTENSITY ANALYSIS OF CAROTID ARTERIES IN IDENTIFYING AND MONITORING LEFT VENTRICULAR SYSTOLIC FUNCTION DYNAMICS IN RABBITS

HUI ZHANG,* RONGQIN ZHENG,* XIAOXIAN QIAN,† CHENGXI ZHANG,† BAOSHUN HAO,† ZEPING HUANG,* and TAO WU*

*Department of Ultrasound, Third Affiliated Hospital of Sun Yat-Sen University, Institute of Diagnostic and Interventional Ultrasound, Sun Yat-Sen University, Guangzhou, China; and †Department of Cardiology, Third Affiliated Hospital of Sun Yat-Sen University, Guangzhou, China

(*Received* 14 *January* 2013; *revised* 4 *October* 2013; *in final form* 13 *October* 2013)

Abstract—Wave intensity analysis (WIA) of the carotid artery was conducted to determine the changes that occur in left ventricular systolic function after administration of doxorubicin in rabbits. Each randomly selected rabbit was subject to routine ultrasound, WIA of the carotid artery, cardiac catheterization and pathologic examination every week and was followed for 16 wk. The first positive peak (WI_1) of the carotid artery revealed that left ventricular systolic dysfunction occurred earlier than conventional indexes of heart function. WI_1 was highly, positively correlated with the maximum rate of rise in left ventricular pressure in cardiac catheterization ($r = 0.94$, $p < 0.01$) and moderately negatively correlated with the apoptosis index of myocardial cells, an indicator of myocardial damage ($r = -0.69$, $p < 0.01$). Ultrasound WIA of the carotid artery sensitively reflects early myocardial damage and cardiac function, and the result is highly consistent with cardiac catheterization findings and the apoptosis index of myocardial cells. (E-mail: zhengrongqin123@163.com) **© 2014 World Federation for Ultrasound in Medicine & Biology.**

Key Words: **Wave intensity, Carotid artery, Echocardiography, Left ventricular systolic function, Ejection fraction.**

INTRODUCTION

Myocardial damage can cause left ventricular systolic dysfunction and can eventually lead to left heart failure. Therefore, assessment of left ventricular systolic function is helpful in understanding the extent of cardiac damage, informing treatment choices and evaluating outcomes. At present, non-invasive techniques for the evaluation of left ventricular systolic function include cardiac computed tomography (CT), magnetic resonance imaging, radionuclide imaging and cardiac ultrasound. Because of the higher resolution and availability of imaging techniques, cardiac CT and magnetic resonance imaging are used to calculate left ventricular ejection fraction (LVEF). In addition to this calculation, cardiac radioisotope scanning can be helpful in understanding the metabolic status of the heart. However, these tests are somewhat limited because they (i) are expensive, (ii) are inapplicable to patients with metal grafts implanted or (3) pose the risk of radiation exposure (single-photon-emission computed tomography and CT scans) (Bandettini and Arai 2008; Dudka et al. 2009; Jurcut et al. 2008; Monsuez 2012; Pongprot et al. 2012; Trachtenberg et al. 2011; Vogel-Claussen et al. 2006). Echocardiography is a non-invasive, radiation-free, simple and cost-effective approach, and is the preferred imaging method for clinical evaluation of left ventricular structure and function (Barry et al. 2007; Geiger et al. 2012; Harake et al. 2012; Thigpen et al. 2012; van der Pal et al. 2012; Zuppinger et al. 2007). Current ultrasound assessment of left ventricular systolic function is measured on the heart itself through the intercostal spaces. However, a limited acoustic window in patients with narrow intercostal spaces, obesity and emphysema and elderly patients can compromise the clarity of ultrasound images, thus affecting the accuracy of the assessment of left ventricular function. Furthermore, LVEF measurements, which are important indicators for assessment of left ventricular

Address correspondence to: Rongqin Zheng, Department of Ultrasound, Third Affiliated Hospital of Sun Yat-Sen University, Institute of Diagnostic and Interventional Ultrasound, Sun Yat-Sen University, Guangzhou, China. E-mail: zhengrongqin123@163.com

systolic function, are largely dependent on cardiac morphologic changes and pre- and afterload, without taking into account the effect of ejection time, leading to a certain degree of bias (Cardinale et al. 2004; Gottdiener et al. 2002; Marwick 2013).

Wave intensity analysis (WIA), a modality developed in recent years, is used to evaluate cardiac function on the basis of peripheral vascular and blood flow parameters (Parker et al. 1988). Instantaneous wave intensity is a new hemodynamic variable that describes the process in which myocardial contraction of the left ventricle gives rise to a forward compression wave spreading and transferring energy from the myocardium to the peripheral arteries. Therefore, the net intensity of such a wave in peripheral arteries reflects the instantaneous state in cardiac contractility under the influence of afterload. Instantaneous wave intensity represents the transfer rate between kinetic and elastic energies of blood flow. Previous studies have found that the waveforms of changes in blood pressure of the carotid artery and vessel diameters are highly correlated (Sugawara et al. 2000). Current ultrasound carotid echo tracking technology can sensitively detect changes in vessel diameter. The echo tracking method can accurately and automatically track and calculate the waveform of diameter changes in response to blood pressure and provide insight into the elasticity of blood vessels. The derivative of changes in local pressure of the carotid artery (dP/dt) can be calculated from measurements of vessel diameter changes. The derivative of changes in blood flow of the carotid artery (dU/dt) can be calculated based on the local flow velocity measured by Doppler ultrasound. Therefore, the WI value can be calculated with the formula $WI = (dP/dt) \times (dU/dt)$.

Many studies have found that the first positive peak (WI_1) of the WI curve is linked to left ventricular systolic function in that the WI_1 peak is decreased when left ventricular systolic function declines and is increased when function strengthens. Also, carotid WIA indicators can be used to assess the prognosis of end-stage cardiomyopathy. In addition to measurements of the instantaneous cardiac state, WIA in peripheral vessels can provide information on the heart and blood vessels, as well as hemodynamic changes caused by myocardial contraction and relaxation (Bjällmark et al. 2011; Jones et al. 2002; Liu et al. 2011; Niki et al. 2002, 2005; Nobuoka et al. 2001; Ohte et al. 2003; Palombo et al. 2009; Siniawski et al. 2002; Takaya et al. 2013).

Although there have been several studies on the relationship between WIA of the carotid artery and cardiac function, further investigations are required for consensus on two issues: (i) "Is WIA of the carotid artery a sensitive method for non-invasive monitoring of early damage and dynamics of left ventricular function?" "Is it better than conventional echocardiography?" (ii) "What is the relationship between cardiac function dynamics assessed by ultrasonic WIA and pathologic findings?"

RESEARCH OBJECTIVE

According to the literature, anthracyclines can cause left ventricular dysfunction. Decline in left ventricular systolic function will lead to a decrease of the positive compression wavefront in vessels. So the peak value of WI_1, which reflects the intensity of the positive compression wavefront, will decrease. A model of rabbits with left ventricular dysfunction after doxorubicin (Adriamycin, ADR) administration was established. WIA of the carotid artery was conducted to determine the changes in left ventricular systolic function before and after administration. WIA was also used to determine the sensitivity of this modality in reflecting early left ventricular systolic dysfunction and its correlation with cardiac catheterization and myocardial pathologic findings.

METHODS

Materials

Eighty healthy New Zealand white rabbits were used in the study, 12 for the pilot experiment and 68 for the actual study The rabbits were provided by the Experimental Animal Center of Guangdong Province (Animal Quality Certification No. 0046418, Animal Facility Use certificate No. SYXK [Guangdong] 2007-0081). The rabbits were about 4 mo old and weighed approximately 2–2.5 kg (2.3 ± 0.2 kg). Hydrochloric ADR powder (10 mg/bottle, Batch No. 080602, Meiji Pharmaceutical, Shantou Special Economic Zone, Shantou City, Guangdong Province, China) was used in the study and diluted in normal saline to 1 mg/mL before use. The study was approved by the Committee of Animal Use and Ethics of Sun Yat-Sen University. All procedures complied with the U.S. National Institutes of Health's *Guide for the Care and Use of Laboratory Animals*.

Model of heart damage

An intravenous injection was administered once every week for 8 wk. Treatment was then stopped, and cardiac function was monitored for 8 wk, in accordance with previous reports (Arnolda et al. 1985; Breed et al. 1980). Rabbits were weighed before each injection. The dosage of the intravenous injection was 2 mg/kg; the total dosage over 8 wk amounted to 16 mg/kg.

All rabbits were raised separately in single cages and fed on demand in the Experimental Animal Center of Sun Yat-Sen University. Rabbits were closely observed for fatigue, anorexia and obvious weight loss, without special treatment. In the event of diarrhea, berberine was administered as a symptomatic treatment. Rabbits that died