QPV Interval as a Measure of Arterial Stiffness in Women with Systemic Lupus Erythematosus

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ABSTRACT

Background: Systemic lupus erythematosus (SLE) is associated with premature atherosclerosis and increased arterial stiffness. The QPV interval has been proposed as a measure of arterial stiffness. The QPV interval is based on the premise that transit time from cardiac ejection to brachial artery flow is shortened in patients with increased arterial stiffness.

Hypothesis: The objective of this study was to determine the significance of the QPV interval as a measure of arterial stiffness in patients with SLE.

Methods: We prospectively studied 46 female SLE patients. The QPV interval was calculated as the time from onset of the QRS complex to peak flow velocity of the brachial artery during ultrasound examination. Measurements of arterial stiffness: augmentation index (AI) and pulse wave velocity (PWV) were obtained by applanation tonometry while patients were on a stable medical regimen.

Results: Mean age was 44±14 y and mean QPV interval was 198±18 msec QPV interval correlated inversely with age ($r = -0.39$, $p = 0.008$), AI ($r = -0.41$, $p = 0.004$), PWV ($r = -0.39$, $p = 0.007$), and aortic pulse pressure (PP) ($r = -0.45$, $p = 0.002$). On multivariate regression analysis, QPV interval was found to be an independent predictor of PWV after adjusting for age ($R^2 = 0.26$, $p<0.001$).

Conclusion: In women with SLE, QPV decreases with age and is inversely related with measures of arterial stiffness. QPV may be useful in identifying SLE patients with higher arterial stiffness in the clinical or research setting. Further larger studies are needed to confirm these preliminary results.

Key words: arterial stiffness, QPV interval, systemic lupus erythematosus

Introduction

Systemic lupus erythematosus (SLE) is associated with premature atherosclerosis and increased arterial stiffness.[1–6] Increased arterial stiffness is an independent predictor of increased risk for future cardiovascular events.[7] A variety of techniques are available to measure arterial stiffness.[8] Recently, the QPV interval, derived from Doppler ultrasound of the brachial artery, has been proposed as a new measure of arterial stiffness.[9] The QPV interval is based on the premise that the transit time from cardiac ejection to brachial artery flow is shortened in patients with increased arterial stiffness. This prior study by Lee et al. was designed to determine the validity of the QPV interval in patients with hypertension. The QPV interval was found to be inversely associated with age, systolic blood pressure, and peripheral pulse pressure (PP). The QPV interval was also shown to inversely correlate with brachial ankle pulse wave velocity (PWV), derived by volume plethysmography.[9]

In recent years, assessment of endothelial function by brachial artery ultrasound has grown in the research settings.[10] Brachial artery Doppler flow is routinely recorded during endothelial function assessment. From a technical standpoint, brachial artery Doppler flow is relatively easy to assess, and its simultaneous recording with the QRS complex allows for measurement of the transit time from cardiac ejection to brachial artery flow. The objective of the present study was to determine the significance of the QPV in patients with lupus. We compared the QPV interval directly with established measures of arterial stiffness.

Methods

The institutional review board approved the study and written consent was obtained from the participating subjects. We prospectively studied 46 women with SLE. Clinical data including past medical history, smoking status, and medications were obtained from patient interview and chart review. Patients were included if they were clinically stable for 6 mo on a constant medical regimen and had adequate pulses for arterial tonometry measurements. Patients were excluded if they had atrial fibrillation or were not in sinus rhythm, or if they had a history of arterial thrombosis. The risk factors evaluated in this study included age, hyperlipidemia, diabetes mellitus, hypertension, body mass index (BMI), and

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smoking status. Smokers were defined as patients using at least 1 cigarette daily. Hypercholesterolemia, hypertension, and diabetes mellitus were defined either as self-reported, documented diagnosis obtained from chart review, or current treatment with medication. Patient BMI was calculated as the weight in kilograms divided by the square of height in meters.

Measurement of the QPV Interval

All studies were done in a quiet, low-light, and temperature-controlled room in the supine position after a 5-min rest period. Brachial artery ultrasound was performed with a 7.5-MHz linear-array ultrasound probe (Phillips 5500, Phillips, Amsterdam, the Netherlands) on a right arm by a single dedicated physician. The brachial artery was imaged above the antecubital fossa in the longitudinal plane. Electrocardiogram (ECG)-gated Doppler spectral flow velocity signal was obtained from a mid-artery sample volume. The QPV interval was measured according to the previously published method as the time intervals expressed in milliseconds between the onset of the QRS complex and the peak brachial artery Doppler flow velocity.[9] The time intervals measured at 3 consecutive velocity waveforms were averaged. The intraobserver and interobserver coefficients of variation between measurements of QPV interval were 6.2% and 5.7%, respectively.

Measurement of Arterial Stiffness

Arterial stiffness was evaluated by measuring augmentation index (AI) and PWV by applanation tonometry. We used an applanation tonometer interfaced with SphygmoCor software, version 6.2 (AtCor Medical, New South Wales, Australia). The central aortic pressure waveform and AI were derived from the radial artery waveform by a validated and population-based generalized transfer function.[11] The AI was defined as the proportional increase in systolic pressure due to the reflected wave and was expressed as a percentage of the PP.[12] The AI was corrected to a heart rate of 75 beats/min.[13] Only high-quality recordings, defined as an in-device quality index >80% and confirmed by visual analysis were analyzed. Sequential recordings of arterial pressure waveform at the carotid and radial arteries measured aortic PWV. Distances from the suprasternal notch to the carotid sampling site (distance A) and from the suprasternal notch to the radial artery (distance B) were measured. The PWV distance was calculated as distance B minus distance A. Aortic PWV was calculated as the ratio of the distance in meters to the transit time in seconds.[12] In addition, arterial stiffness was assessed by measuring the aortic PP derived from the radial artery waveform.

Statistical Analysis

All values are expressed as mean±standard deviation. Univariate associations between study variables were analyzed using Spearman's correlation coefficients. Continuous data were compared using a Student *t*-test. Forced multivariate linear regression was used to determine independent correlates of PWV. All statistical analyses were achieved using the Statistical Package for Social Sciences (SPSS) 15.0 software (SPSS Inc., Chicago, Ill., USA). A p-value <0.05 was considered statistically significant.

Results

Patient characteristics are shown in Table 1. There were 46 females, age 44±14 y. The majority of patients were African American (82.6%). Mean QPV interval was 198±18 msec. The QPV interval correlated inversely with age ($r = -0.39$, $p = 0.008$), AI ($r = -0.41$, $p = 0.004$), AI 75 ($r = -0.41$, $p = 0.003$), PWV ($r = -0.39$, $p = 0.007$), and aortic PP ($r = -0.45$, $p = 0.002$) (Figure 1). Mean QPV interval was lower in patients with hyperlipidemia (187±26 msec versus 203±12 msec, $p = 0.006$). The QPV interval was lower in patients with diabetes (189±18 msec versus 200±18 msec, $p = 0.12$), but did not reach statistical significance. The QPV interval was similar among the hypertensive and non-hypertensive groups (193±23 msec versus 201±13 msec, $p = 0.20$). On multivariate regression analysis, the QPV interval was found to be an independent predictor of PWV after adjusting for age ($R^2 = 0.26$, $p<0.001$). There were no significant relationships between QPV interval and either height ($r = 0.17$, $p = 0.27$), BMI ($r = -0.02$, $p = 0.89$), or heart rate ($r = 0.12$, $p = 0.44$). Mean QPV interval was similar among patients who were and were not treated with steroids (198±18 msec versus 199±19 msec, $p = 0.89$). There was no difference in the QPV interval (197±22 msec versus 201±15 msec, $p = 0.58$), PWV (9.4±1.2 msec versus 9.0±1.6 msec, $p = 0.43$), AI (27.6±14.2 msec versus 22.0±13.9 msec, $p = 0.21$), or AI 75 (24.3±12.0 msec versus 21.4±12.6, $p = 0.47$) between patients taking or not taking angiotensin-converting enzymes inhibitors. In patients treated with beta-blockers there was a trend toward lower QPV (187±25 msec versus 203±12 msec, $p = 0.06$) and higher aortic PP (44±17 mm Hg versus 33±8 mm Hg, $p = 0.053$), but no significant differences in PWV (9.4±2.1 msec versus 9.0±1.2 msec, $p = 0.48$), AI (28.6±15.4 msec versus 21.9±13.4 msec, $p = 0.19$), or AI 75 (25.9±13.7 msec versus 20.9±11.7 msec, $p = 0.26$) at similar heart rates (69±10 bpm versus 73±9 bpm, $p = 0.23$).

Discussion

Chronic inflammatory diseases are associated with premature atherosclerosis and increased arterial stiffness. Reliable and easily obtainable measures of stiffness are desirable.[4] In this study of predominantly African American women with lupus, the QPV interval, a recently proposed measure of arterial stiffness, was measured using brachial artery ultrasound and compared to accepted indices of arterial stiffness. We did not compare our SLE cohort to normal controls because

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it is well known that SLE and African American ethnicity are associated with increased arterial stiffness.[2–4,6] The QPV interval was inversely correlated with aortic PP, AI, and PWV standard measures of arterial stiffness. As expected, the QPV interval decreased with older age and with hyperlipidemia. After adjusting for age, a known determinant of arterial stiffness, the QPV interval remained significantly correlated with PWV. These results are similar to those of Lee et al., who compared the brachial-to-ankle PWV using volume plethysmography to the QPV interval in hypertensive and nonhypertensive normal subjects.[9] Mean QPV values were similar to the QPV values reported in that study. The lack of an association of the QPV interval with height and heart rate was also noted previously.[9] In the present study, the QPV interval was similar in patients taking and not taking steroids, analogous to prior studies that demonstrated steroid use to have no effect on arterial stiffness.[2]

The QPV interval represents the transit time from cardiac ejection to brachial artery flow. In general, studies using arterial pressure waveforms have found shortened transit times in patients with increased arterial stiffness. The QPV interval is measured from the Q wave of the ECG to the peak of the brachial artery Doppler waveform. The QPV interval includes the pre-ejection period, or the initiation of electrical activity to the initiation of ejection, and the pulse wave transit time to the brachial artery. The pre-ejection period may vary depending on left ventricular function, blood pressure and QRS duration.[14,15] In patients with left bundle-branch block (LBBB) the pre-ejection period is prolonged. In the present study, the QRS duration was evaluated via the monitor lead, and no subject was believed to have QRS prolongation. The QPV interval and arterial stiffness measurements were done simultaneously to avoid variation in blood pressure. Also, it is known that the left ventricular outflow tract Doppler-derived time to peak velocity, or acceleration time, may vary according to left ventricular function.[16] It is not known if blood flow acceleration in the brachial artery changes with varying left ventricular function or hemodynamic conditions. Left ventricular function, a potential confounder in the evaluation of arterial stiffness, was not evaluated. Our results indicate the QPV interval correlates with PWV and AI regardless of left ventricular function; however, the relationship between the QPV interval and left ventricular function merits further study.

It has been reported that there may be time differences in ECG data and ultrasound data displayed on the ultrasound machine oscilloscope.[15,17] This may vary between different machines, and even vary when data are displayed on a frozen video frame versus a live recording. These factors may impact on measurements if absolute timing is required, if more than 1 ultrasound machine is used, or if different methodologies to measure time intervals are employed. In our study, 1 ultrasound machine was used for time measurements, and measurements were made using the same methodology. Amato and Shamoon have noted that measuring the pulse transit time to the brachial artery from the heart using the peak of the left ventricular outflow tract Doppler rather than the Q wave of the ECG complex may reduce concerns regarding machine-processing errors and the pre-ejection period.[15] This concept merits further investigation.

We found no difference in the QPV interval or other stiffness measures in patients taking angiotensin-converting enzymes inhibitors. We did note a trend toward a lower QPV and higher aortic PP in patients taking beta-blockers. The AI appeared generally higher in the beta-blocker group; however, this was not statistically significant. This is in line with other studies that suggest central aortic pressure may

TABLE 1: Patient characteristics

Age	44±14 y
Female	100%
African American	82.6%
Hypertension	39.1%
Diabetes	17.4%
Smoking history	6.5%
Hyperlipidemia	28.3%
Height	1.62±0.05 m
Weight	74.2±16 kg
Body mass index	27.8±6.1 kg/m^2
Heart rate	72±9 bpm
Systolic blood pressure	148±20 mm Hg
Diastolic blood pressure	86±10 mm Hg
Medications	
Steroids	56.5%
Immunosuppressive	78.3%
Hormone replacement therapy	4.3%
Angiotensin-converting enzyme inhibitors	32.6%
Beta-blockers	26.1%
Statins	19.6%
Aortic pulse pressure	35±10 mm Hg
Pulse wave velocity	9.2±1.5 msec
Augmentation index	23%±14%
QPV	198±18 msec

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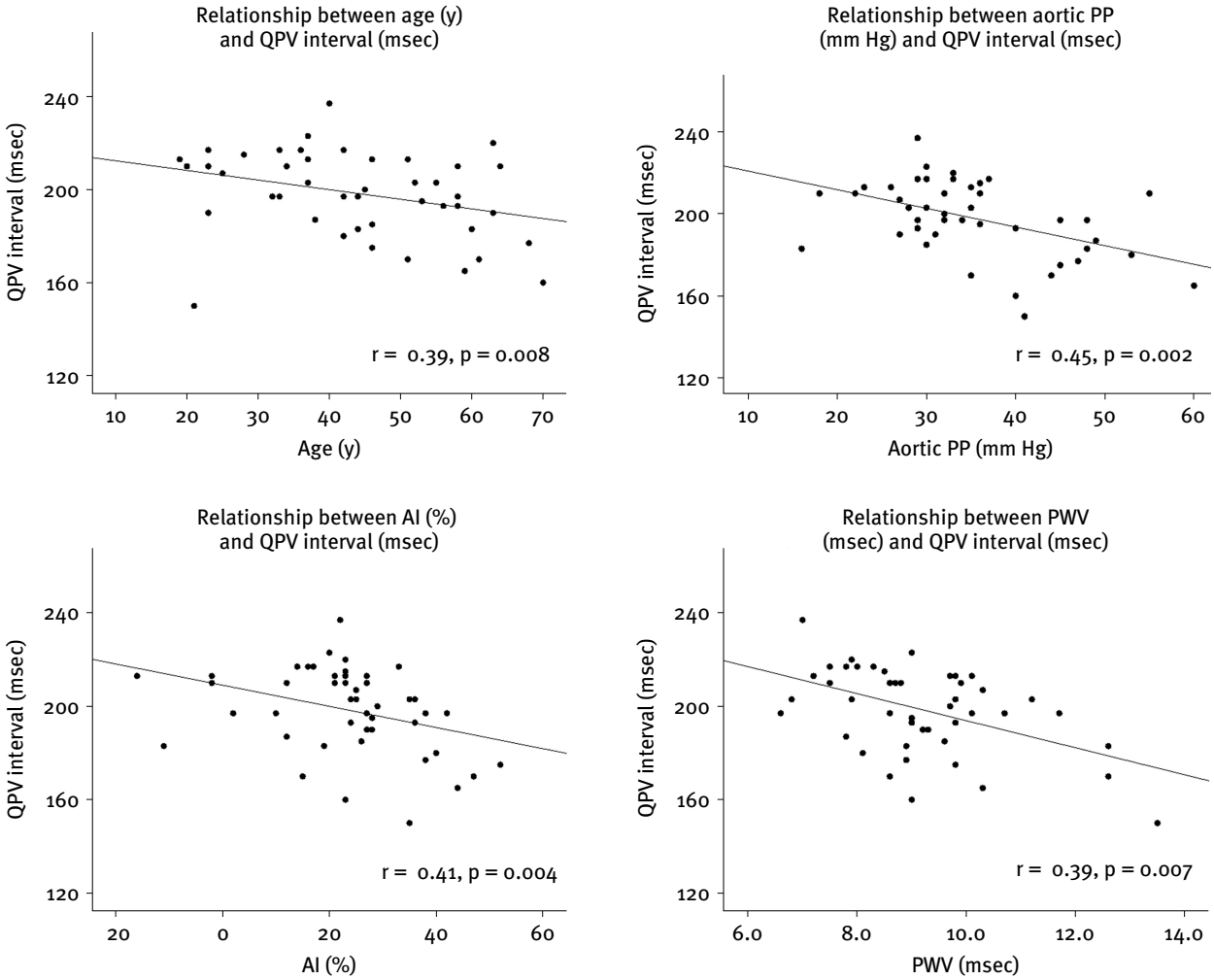

Figure 1: Relationships between QPV interval and age, aortic PP, AI, and PWV.

not decrease significantly with beta-blockers, and that aortic wave reflection may actually increase.[18] However, the size of our patient sample was too small to adequately evaluate medication effects.

Limitations

This study was limited by its relatively small sample size; however, it confirms the relationship of the QPV interval and arterial stiffness in a population different from the prior study by Lee et al.[9] Too few patients who had anticardiolipin antibodies were treated with hormone replacement therapy or were not treated with immunosuppressive agents to assess the effects of these exposures on the QPV interval. Medication effects on the QPV interval could not be fully evaluated due to small sample size. The effects of beta-blockers and vasodilators need further study. Nitroglycerin was not administered. Although nitroglycerin has been shown to increase the QPV interval, prior associations between QPV were determined at baseline and not after administering nitroglycerin.[9] The prognostic value of QPV remains to be determined.

Conclusion

In women with SLE, the QPV interval decreases with age, is associated with hyperlipidemia, and is inversely correlated with PWV, AI, and aortic PP. Therefore, measurement of the QPV interval may serve as a measure of increased arterial stiffness alone or in conjunction with assessment of endothelial function using brachial artery ultrasound in patients with SLE, or in patients with other chronic inflammatory diseases. Future prospective studies are needed to confirm these preliminary results.

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