

LETTER TO THE EDITOR

Assessment of cardiovascular risk in type 2 diabetes patients by insight into radial pulse wave harmonic index

To the editor: An article recently published by Professor Wang Lin provides an insightful explanation as to why the harmonic components of radial pulse waves may be an important set of signs to reveal the state of the ventricular-arterial system.¹ The important basis of the article comes from the "resonance theory" proposed by Wang et al through a series of elegant animal studies.^{2,3} Here, we would like to provide further clinical references to point out the important correlation between the harmonic components of the radial pulse wave and the risk of future cardiovascular events.

In 2017, we initiated an observational cohort study of RPWT2DM (IRB number: ISRCTN14306167) for cardiovascular risk assessment in patients with type 2 diabetes using radial pulse measurements. We found that the first harmonic amplitude (C1), the second harmonic phase (P2) and the variation coefficient of fourth harmonic amplitude (C4CV) of radial pulse wave are related to cardiovascular risk. The first cross-sectional survey showed that patients with more than 5% of ischaemic myocardium had higher C1 and C4CV than those without myocardial ischaemia.⁴ In this cross-sectional study, we also found that patients with a left ventricular ejection fraction of less than 50% had higher C1, higher C4CV and lower P2 compared to patients with normal cardiac function. After a mean of 1.8 years of follow-up, we found a clearer association between these indicators and the risk of cardiovascular events. Cox proportional hazards model demonstrated that C1 is an independent predictor for major adverse cardiovascular events,⁵ cardiovascular mortality⁶ and microvascular events.⁶ The results also demonstrate that C4CV is independently and positively correlated with macrovascular and microvascular events.⁷ Macrovascular events combined the major adverse cardiovascular events, coronary artery disease and severe peripheral artery disease. Microvascular events combined the major adverse kidney events, macroalbuminuria, retinopathy and polyneuropathy. In addition, we demonstrate that lower quartile levels of P2 values can independently predict an increased risk of macrovascular and microvascular outcomes.⁸

Based on the above studies, we determined three harmonic characteristics (C1 > 1.07, C4CV > 13% and P2 < 3.54) with high cardiovascular risk. In the RPWT2DM study, 556 (24%), 270 (12%) and 119 (5%) type 2 diabetic patients respectively, had 1, 2 and 3 cardiovascular risk-related harmonic characteristics as described above. One thousand three hundred and seventy-nine (59%) of those patients did not have any of the above

harmonic characteristics. We performed a Cox proportional hazard model to determine the hazard ratios (HRs) between them. Compared with those without any high-risk harmonic pattern, patients with two of three high-risk harmonic characteristics had an approximately 80% increase in the incidence of microvascular events (HR, 1.76; 95% CI 1.44-2.16), and had more than doubled incidence of major adverse cardiovascular events (HR, 2.23; 95% CI 1.75-2.86) and macrovascular events (HR, 2.31; 95% CI 1.88-2.85). In addition, with reference to patients with normal harmonic patterns, the HRs for patients with three high-risk harmonic characteristics (C1 > 1.07, C4CV > 13% and P2 < 3.54) are listed below: major adverse kidney events (HR, 2.64; 95% CI 1.92-3.64), macrovascular events (HR, 2.56; 95% CI, 1.93-3.39) and macrovascular events (HR, 2.43; 95% CI, 1.88-3.13). Furthermore, 49% and 59% of patients with all these high-risk harmonic characteristics at baseline experienced at least one macrovascular and one microvascular event respectively during a mean follow-up of 2.3 ± 0.5 years.

The above results indicate the great potential for cardiovascular risk assessment using radial pulse harmonic predictors. These results are consistent with Lin Wang's theory and inference.¹ We hope that this letter will trigger more discussion and investigation on underlying mechanisms of how the radial pulse wave harmonics reflect the cardiovascular event development, which may open up new perspectives for cardiovascular event prevention strategies.

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REFERENCES

1. Lin Wang Y-Y. Did you know developing quantitative pulse diagnosis with realistic hemodynamic theory can pave a way for future personalized healthcare. *Acta Physiol.* 2019;227(3):e13260.
2. Lin Wang Y-Y, Chang S-L, Wu Y-E, Hsu T-L, Wang W-K. Resonance - the missing phenomenon in hemodynamics. *Circ Res.* 1991;69:246-249.
3. Young S-T, Wang W-K, Chang L, Kuo T-S. The filter properties of the arterial beds of organs in rats. *Acta Physiol Scand.* 1992;145:401-406.
4. Liao K-M, Chen Y-C, Wang S-H, Wang G-C, Chang C-W. Harmonics of the radial pulse could be risk factors for myocardial ischemia and decrease of heart function in patients with type 2 diabetes. *J Diabetes Investig.* 2018;9(suppl 1):38.
5. Chang C-W, Liao K-M, Chang Y-T, Wang S-H, Chen Y-C, Wang G-C. The effect of radial pulse spectrum on the risk of major adverse cardiovascular events in patients with type 2 diabetes. *J Diabetes Complicat.* 2018;33(2):160-164.
6. Liao K-M, Chang C-W, Wang S-H, Chang Y-T, Chen Y-C, Wang G-C. The first harmonic of radial pulse wave predicts major adverse cardiovascular and microvascular events in patients with type 2 diabetes. *J Diabetes Complicat.* 2019:107420. <https://www.sciencedirect.com/science/article/abs/pii/S105687271930738X>
7. Liao K-M, Chang C-W, Wang S-H, Chang Y-T, Chen Y-C, Wang G-C. Risk assessment of macrovascular and microvascular events in patients with type 2 diabetes by analyzing the amplitude variation of the fourth harmonic component of radial pulse wave. *Physiol Rep.* 2019;7:e14252.
8. Chang C-W, Liao K-M, Wang S-H, Chang Y-T, Chen Y-C, Wang G-C. The phase of second harmonic of radial pulse wave predicts the macrovascular and microvascular outcomes and mental disorder in asymptomatic patients with type 2 diabetes. Paper presented at. No. 9970, American Heart Association Scientific Sessions. 2019.