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Original Article

Noninvasively measured radial pressure wave analysis provides insight into cardiovascular changes during pregnancy and menopause

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ABSTRACT

Objective: Pregnancy and menopause are significant life events associated with major changes in female hormone levels and changes in cardiovascular health. The role of estrogen in influencing cardiovascular risk is an ongoing research topic. Many studies have provided evidence that radial pressure wave characteristics are an important indicator to consistently and independently predict cardiovascular events. The aim of this study was to investigate if radial pressure wave analysis provided statistical insights into the physiological variations due to pregnancy and menopause. Furthermore, the study investigated how these variations could serve as an indicator for cardiovascular risks. As the radial pulse measurement is non-invasive and speedy, it may be helpful in evaluating cardiovascular changes and risk during these transitions.

Materials and method: A total of 702 randomly selected female subjects (90 pregnant and 97 postmenopausal), aged 20–59, enrolled in the study. The visit measured the subject's hemodynamic parameters including heart rate, systolic blood pressure (SBP), diastolic blood pressure (DBP) and radial pressure waves. SBP and DBP were evaluated by an automatic blood pressure monitor. Radial pressure wave data were continuously recorded for 12-s using a TD01C pulse measuring instrument. Spectrum analysis of the radial pressure wave was performed to evaluate the first five harmonic components (C1–C5).

Results: A comparison of pregnant women to non-pregnant women showed C3 and C5 were lower. Heart rate C2 and C4 were higher in pregnant women. A comparison of women pre-menopausal and postmenopausal showed no significant difference in SBP or DBP. Menopause significantly changed the C1 and C4 radial pressure wave harmonics. An increase in C1 and a decrease in C4 were observed.

Conclusion and discussion: This study provided further clinical evidence to support the hemodynamic model that describes the cardiovascular changes and risks related to the harmonic components of the pulse spectrum. Beyond blood pressure, the effects of menopause on the radial pressure wave, especially on hemodynamic index C4, independent of age and BMI, may explain increased post-menopausal cardiovascular risk. This and past studies collectively suggest that radial pressure wave components may be an indicator of a female body's ability to supply oxygen and nutrients. Harmonic analysis of the radial pressure wave may provide additional insights into the underlying mechanism of the cardiovascular changes over the lifespan of a woman.

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Introduction and objectives

Cardiovascular diseases (CVD) are the leading cause of death for women over 65 and the second leading cause of death among women ages 45 to 64. Recently, researchers have found that age at menopause is an important factor in risk stratification of cardiovascular disease for women [1]. However, the greater incidence of cardiovascular disease in postmenopausal women could not be explained by the influence of the menopause on the usual cardiovascular risk factors [2]. Pregnancy is the other important stage associated with cardiovascular adaptation. Non-invasive monitoring of the hemodynamic status of pregnant women may provide additional information on whether sufficient nutrients and oxygen are provided for the developing fetus.

Pulse waveform of radial pressure wave describes the change of the arterial pressure over time. Harmonic analysis transforms the waveform into harmonic indexes and provides hemodynamic information of the condition of ventricular-arterial system [3–6]. Changes in blood flow [7,8] and the functioning [9] of organs will alter the waveform of the radial pulse wave [3]. Many studies have demonstrated that radial pulse waves provided independent predictive value for cardiovascular variations [10–13]. Our previous studies have shown that the harmonic components of the radial pressure wave are associated with cardiovascular events [14–16]. Specifically, decreasing of the fourth harmonic of radial pulse wave (C4) predicts adverse cardiac events in asymptomatic patients with type 2 diabetes [14].

The harmonic components of radial pressure waves may be a missing piece to inform the state of the ventricular-arterial system during pregnancy and menopause. This study aimed to investigate the specific statistical relationship of the changes of radial pressure wave during menopause and pregnancy. The simple radial pulse measurement may provide additional cardiovascular insights during these transitions.

Method

This three-year study included 702 female subjects, aged 20–59 and without cardiovascular history or hormone replacement therapy, at the Department of Gynecology and Obstetrics of the Renai Branch of Taipei City Hospital starting from 2017. All participants provided a written informed consent. The study protocol followed good clinical and scientific practice. And was approved by the Institutional Review Board of Taipei City Hospital (IRB number: ISRCTN20480882). All population were separated to the dataset of pregnancy group and dataset of perimenopause group, according to age, pregnancy status and menopause status.

Harmonic analysis

Each subject was asked to rest for 5 min. The radial pressure wave was recorded on the radial artery with a pulse wave analyzer (TD01C, MII-ANN Technology, Taiwan). The TD01C is an accurate instrument which proved its intrinsic reliability using an artificial pulse generator [17]. The continuous pulse data was collected in 12 s with a sampling rate of 400 data points per second. After completing the radial pulse wave measurement, the blood pressure and heart rate of each subject were measured using an automatic blood pressure monitor (EASYX800R, JAWON Medical, Korea). A trained operator conducted blood pressure measurements and instructions were followed to avoid the white coat effect.

Harmonic components were then calculated using the Fourier transformation:

$$C_n = \frac{1}{M}\sum_{m=1}^{M}\frac{A_{n,m}}{A_{0,m}}$$

where $1 \leqq n \leqq 5$, and $A_{i,m}$ $A_{i,m}$ Ai,mAi, m was the ith amplitude coefficient of Fourier series of the mth radial pulse in one measurement, $A_{0,m}$A0,mA0,m is the mean value of the mth radial pulse, and M is the total number of consecutive pulses in the 12 s measurement. Finally, the result Cn. CnCn was denoted as the ith harmonic component.

In addition to the harmonic components (Cn, n = 1–5), other demographic characteristics and hemodynamic variables were also recorded, including age, body mass index (BMI), diastolic blood pressure (DBP), systolic blood pressure (SBP) and heart rate (HR).

With the non-pregnancy data from 612 subjects of all ages, harmonic components well as other hemodynamic variables have shown the significant association with age. While the negative relation exists between age and some harmonic components (C2, C3 and C4), some harmonic components (C1 and C5) are positive correlated with age (Table 1).

Analysis groups

To investigate whether the radial pressure waves are differentiated and potentially provides the insight into cardiovascular changes during pregnancy and menopause, the data was further categorized into pregnancy and perimenopause subgroups (Fig. 1). None of the subjects was diagnosed with cardiovascular diseases during the study.

The pregnancy status was diagnosed by a specialist doctor and confirmed from the ICD-10 codes [18], O, Z32.1 and Z34, on the medical record. The dataset coded with O00 were from those subjects who experienced complications of pregnancy, such as an ectopic pregnancy, and these data were excluded in the analysis. In the perimenopause group, the physician determined each subject's menopause status and excluded pregnancy female. Student's t-test was used to evaluate the difference of basic demographic information and hemodynamic variables based on the status.

Pregnancy group

The pregnancy group category compared the hemodynamic characteristics of women who were not pregnant to those who were pregnant. The dataset for the pregnancy group was composed of 420 subjects within the child-bearing ages of 20–44, none of

Table 1
Correlation between age and harmonic components of radial pulse wave (N = 612).

Variables	*Age (20 − 59)*		
	Pearson's Correlation Coefficient	95% Confidence Interval	*P*
BMI (kg/m^2)	0.131*	(0.055, 0.206)	0.001
DBP (mmHg)	0.143*	(0.048, 0.235)	0.003
SBP (mmHg)	0.270*	(0.179, 0.356)	<0.001
HR (beats/1 min)	−0.141*	(-0.216, −0.065)	<0.001
C1	0.480*	(0.419, 0.537)	<0.001
C2	−0.307*	(-0.375, −0.235)	<0.001
C3	−0.356*	(-0.422, −0.287)	<0.001
C4	−0.109*	(-0.185, −0.033)	0.005
C5	0.176*	(0.101, 0.250)	<0.001

SBP = Systolic blood pressure, DBP = Diastolic blood pressure, HR = heart rate. C1–C5 = Harmonics Indexes. Asterisks indicate that the variables in non-pregnant group are significantly correlated with age ($P \leq 0.01$).

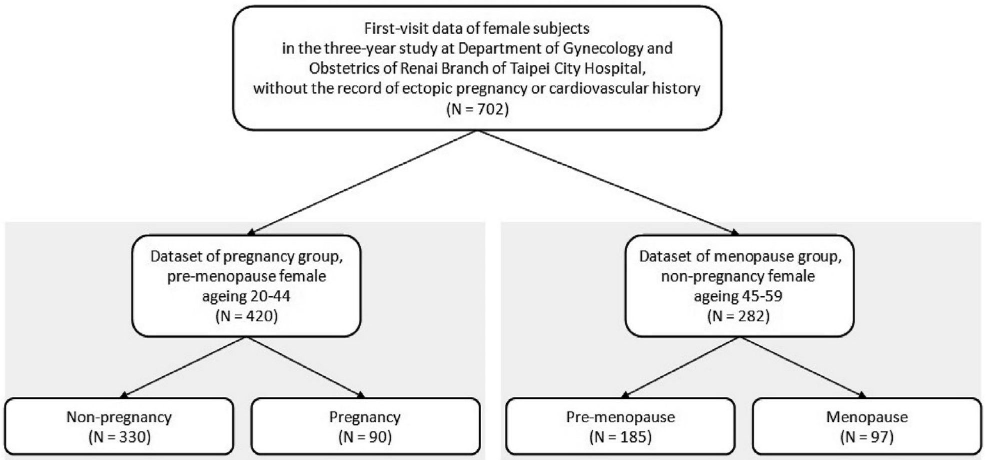

Fig. 1. Enrollment of study participants.

whom were at menopause. The pregnancy group was slightly younger than the non-pregnancy group (Table 2).

Perimenopause group

The perimenopause group category compared the hemodynamic characteristics of women who were pre-menopause to those who were post-menopause. None of the subjects was under hormone replacement therapy during or prior to the study. The dataset includes 282 female subjects aged 45 to 59, none of whom were pregnant. Age was significantly different between pre-menopause and post-menopause (Table 3). We further narrowed down the age to between the age 45 and 49 in the perimenopause group with total of 74 subjects with 13 of them were post menopause to see if it yields the similar results (Table 4).

Results

Pregnancy group

During the pregnancy, the subject's hemodynamic data were measured at the first visit during the study and the subjects can be at different stage of the pregnancy. Our preliminary publication showed that a series of changes in maternal hemodynamic status could be observed during the pregnancy, including lowering blood pressure, increasing heart rate and changing harmonics of radial pulse. Although the stage of pregnancy has effects on hemodynamic, C4 is significantly different between pregnancy or not in pregnant women in all three trimesters. However, C2 was only significantly increased in second and third trimesters [19].

An increase in HR, also with a statistically significant p-value, was also related to pregnancy. Looking at a comparison of non-pregnant to pregnant results of the radial pressure wave (Fig. 2), the figure showed the mean harmonic component for C2 and C4 increased. The mean harmonic components C3 and C5 showed a decrease in subjects who were pregnant.

Perimenopause group

Decreases in the mean HR, DBP, and SBP provided no statistically significant evidence of a connection between early onset menopause and the traditionally measured hemodynamic parameters. A comparison of the mean harmonic component premenopausal and postmenopausal subjects (Fig. 3), showed the means of harmonic components C1 increased and C4 decreased in subjects who were postmenopausal.

Menopause hemodynamics could differ significantly during the age span 40 to 59 depending on the age of onset of menopause. To eliminate the age factor, we further analyzed the subjects in perimenopause group of age between 45 and 49. In this subset, the only

Table 2
Comparison of the pregnancy group dataset (age 20–44).

	Non-pregnancy (N = 330)	Pregnancy (N = 90)	*P*
Age (years)	33.91 ± 6.71	32.68 ± 4.92	0.11
BMI (kg/m^2)	22.15 ± 3.89	22.69 ± 3.5	0.23
DBP (mmHg)	69.44 ± 10.96	65.75 ± 9.18	0.02
SBP (mmHg)	114.21 ± 16.21	110.06 ± 10.59	0.06
HR (beats/1 min)	76.58 ± 11.45	81.9 ± 13.64*	<0.001
HR_CV	0.05 ± 0.03	0.06 ± 0.03	0.10

DBP = Diastolic blood pressure, SBP = Systolic blood pressure, HR = heart rate, HR_CV = variance of heart rate, Asterisks indicate that the means of variables in pregnant group differ significantly from non-pregnant group ($P \leq 0.01$).

Table 3
Comparison of Perimenopause Group Dataset (N = 282, age 45–59).

	Pre-menopause (N = 185)	Menopause (N = 97)	*P*
Age (years)	49.08 ± 2.77	53.22 ± 4.11*	<0.001
BMI (kg/m^2)	22.73 ± 3.48	22.82 ± 3.57	0.85
DBP (mmHg)	74.04 ± 11.32	72.11 ± 11.18	0.29
SBP (mmHg)	122.87 ± 18.24	118.46 ± 22.3	0.17
HR (beats/1min)	76.77 ± 10.46	74.25 ± 8.85	0.04
HR_CV	0.05 ± 0.03	0.04 ± 0.02*	0.01

DBP = Diastolic blood pressure, SBP = Systolic blood pressure, HR = heart rate, HR_CV = variance of heart rate. Asterisks indicate that the means of variables in perimenopause group differ significantly from non-menopause group ($P \leq 0.01$).

Table 4
Comparison of Perimenopause Group Dataset (N = 74, age 45–49).

	Pre-menopause (N = 61)	Menopause (N = 13)	*P*
Age (year)	47.23 ± 1.37	47.38 ± 1.5	0.72
BMI (kg/m^2)	22.52 ± 3.44	22.57 ± 4.04	0.96
DBP (mmHg)	74.92 ± 12	77.88 ± 12.84	0.54
SBP (mmHg)	124 ± 18.12	126.38 ± 18.3	0.74
HR (beats/1min)	77.31 ± 9.79	77.73 ± 12.01	0.89
HR_CV	0.05 ± 0.02	0.04 ± 0.01	0.17

DBP = Diastolic blood pressure, SBP = Systolic blood pressure, HR = heart rate, HR_CV = variance of heart rate. Asterisks indicate that the means of variables in perimenopause group differ significantly from non-menopause group.

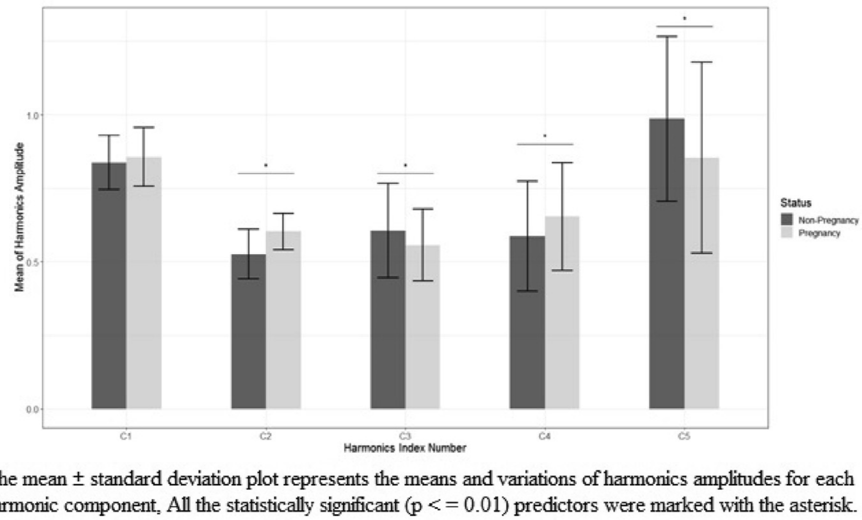

Fig. 2. Pregnancy and non-pregnancy harmonic components (N = 420).

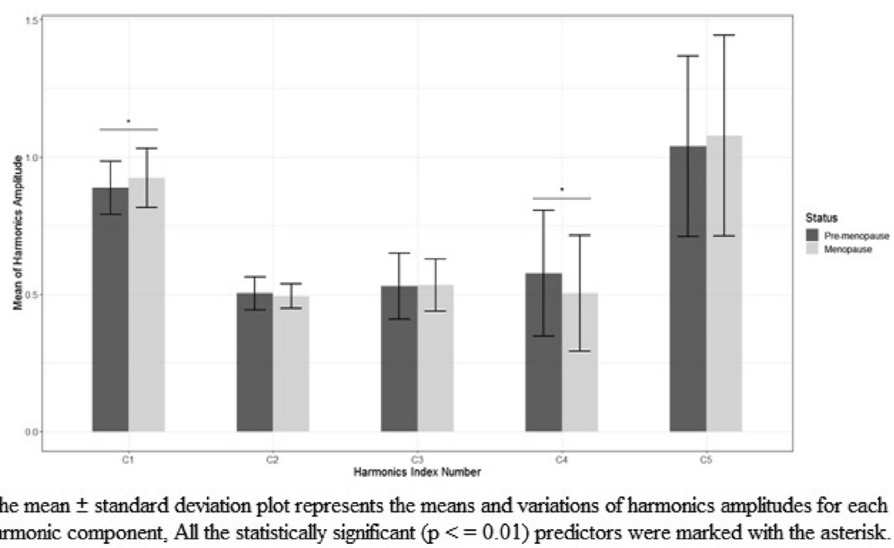

Fig. 3. Pre and post menopause harmonic components (N = 282).

significantly different variable is C4 ($P < 0.05$) (Fig. 4). This indicates that the difference of C4 is not attributed to the age only.

Discussion

Conclusively, this study provided statistical evidence to support that C4 harmonic component of the pulse spectrum had independent value for indicating changes in the female cardiovascular system during pregnancy and menopause.

The role of estrogen in influencing cardiovascular risk is still an ongoing research topic. This study has demonstrated that aging (Table 1), pregnancy and menopause, which are associated with the variations of estrogen, are all related to the fourth harmonic component of the radial pressure wave. Compared with women who were not pregnant, the C4 value of women increased during pregnancy, and the lower C4 value was correlated to aging, as well as the earlier age at natural menopause (Fig. 5). Weber et al. provided evidence that pulse waveform characteristics were an important indicator to consistently and independently predict cardiovascular events [12]. Previous studies, we have also demonstrated that decreasing C4 is associated with atherosclerotic processes and myocardial ischemia in asymptomatic patients with type 2 diabetes and may be an independent predictor of adverse cardiac events [14]. These relations may potentially suggest that C4 is a direct indicator of the health of women's cardiovascular system.

Pregnancy increases the load of the cardiovascular system [20]. During pregnancy, the mother's heart rate and blood volume increases by 30−50 percent to supply more oxygen and nutrients during pregnancy [21]. The persistent C4 increase [19] was observed in maternal hemodynamic changes to support the normal growth of the developing fetus. The DBP decreases observed was consistent with other studies [22]. Invasive measuring techniques are rarely used during pregnancy, so echocardiography is most commonly used to assess hemodynamic in pregnancy [23]. The combination of maternal background and physical findings is also suggested to identify the population with a high risk of hypertensive disorders in pregnancy [24]. Besides, the increase in C2 and C4 occurring at the same time as the decrease in C3 and C5 is a

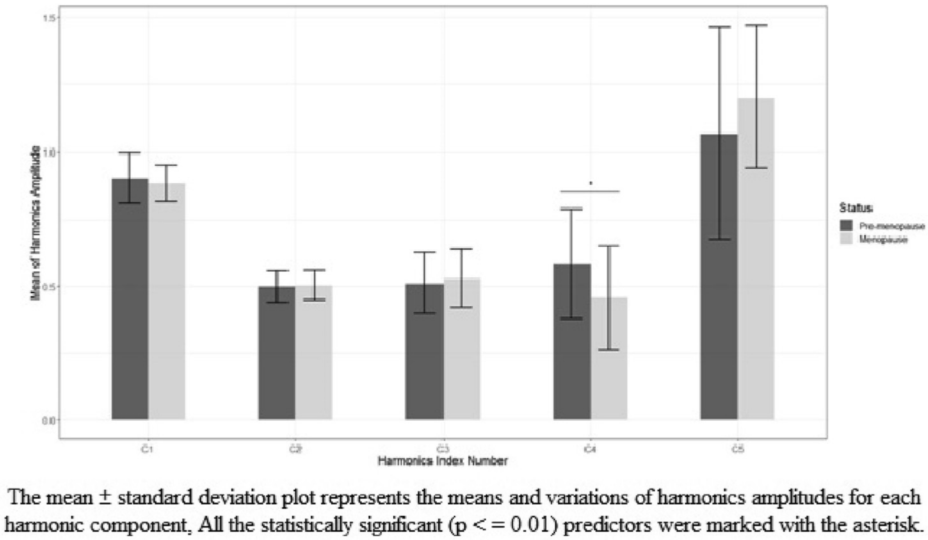

Fig. 4. Pre and post menopause harmonic components (N = 82, age=46 ~ 50).

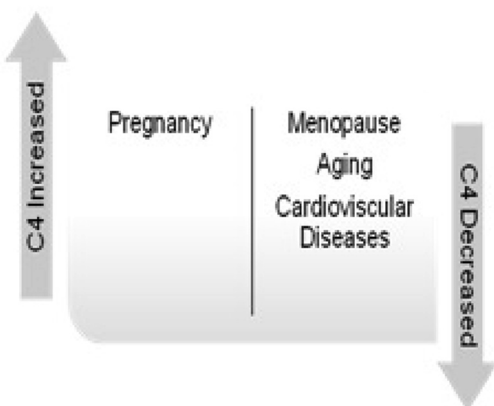

Fig. 5. C4 and menopause, aging, and pregnancy.

characteristic of hemodynamics during pregnancy and may be used as a predictor of pregnancy. In our previous animal study, we found that C3 and C5 are related to the digestive system [7,8]. The reduction of C3 and C5 may provide another hemodynamic explanation for the high risk of diabetes and morning sickness during pregnancy. The simple radial pulse measurement may be performed more frequently and easily. A wearable device with continuous self-monitoring may be possible with the advanced of the technologies.

Aging is a major risk factor for developing cardiovascular disease [25]. When the body is able to increase the body's oxygen and nutrients supply, it is able to sufficiently complete thickening the endometrium. As the body ages matching with the decrease of C4, the body is no longer able to supply enough oxygen and nutrients to complete the cycle of thickening endometrium and menstruation. Therefore, the body goes into the perimenopause phase and eventually experiences menopause. It has been widely recognized that age at menopause is a risk factor for cardiovascular mortality [27]. Women who have an early age at menopause may predict their declined respiratory function and are subjected to higher cardiovascular risks [28–30]. In some studies, it was found that lung disease increased after menopause [26], which also echoed the decrease in C4 observed in this study during menopause. An increase in cardiovascular risk during menopause and the decline of the lung functions may be reflected in the radial pulse spectrum.

An increase in blood pressure is considered an inevitable consequence of aging [31]. The increase in blood pressure is mostly associated with structural changes in the arteries and especially with large artery stiffness [32]. The cardiovascular system delivers oxygen, nutrients, hormones, and other important substances to cells and organs. Due to the coincidence between advancing menopause and aging, the hypothesis that menopause or the estrogen decrease are associated to blood pressure increase is still under debate [33,34]. In our study, age and BMI have an independent effect on SBP, whereas menopause has no significant independent effect on DBP and SBP [35]. The increased cardiovascular risk post menopause may not have direct relationship with blood pressure. Beyond blood pressure, radial pressure wave analysis may provide additional insights into cardiovascular risks post menopause.

Age and menopause are major risk factors for female cardiovascular disease associated with fluctuations of female hormones. Although many studies indicate estrogen exerts beneficial effects on the circulatory system, the overall conclusions from clinical studies remain somewhat equivocal [36]. This study provided a new perspective to understand the relationship between cardiovascular disease and menopause, and harmonic components may be an indicator to reflect the changes in the characteristics of the cardiovascular system. Further studies are required to understand how female hormones may impact hemodynamic indicators, and whether hormonal treatment has an effect on radial pressure waves and the harmonic pulse spectrum. Research on the underlying mechanism of female hormones and their effects on radial pressure waves may advance the understanding of hormones and vascular functions. This understanding will provide a different viewpoint into the outcome of hormone replenishment therapy and a more personalized way [37] to prevent cardiovascular diseases.

Conclusion

Harmonic components of the radial pressure wave provide independent predictive value for changes in the female cardiovascular system during pregnancy and menopause. The noninvasively radial pulse measurement may be performed more frequently and easily. Harmonic components of the radial pressure wave could use in many clinical applications [38]. However regarding the relationship between individual harmonic components and physiology, more experiments are needed to verify in the future.

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Declaration of competing interest

The authors declare that they have no conflicts of interest.

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References

[1] Zhu D, Chung HF, Dobson AJ, Pandeya N, Giles GG, Bruinsma F, et al. Age at natural menopause and risk of incident cardiovascular disease: a pooled analysis of individual patient data. Lancet Public Health 2019;4(11): PE553–64.
[2] Kannel WB, Hjortland MC, McNamara PM, Gordon T. Menopause and risk of cardiovascular disease: the Framingham Study. Ann Intern Med 1976;85(4): 447–52.
[3] Lin Wang YY, Chang SL, Wu YE, Hsu TL, Wang WK. Resonance - the missing phenomenon in hemodynamics. Circ Res 1991;69(1):246–9.
[4] Lin Wang YY, Wang WK. Why the cardiovascular studies should start with the radial oscillation of arterial wall rather than from axial flow motion of blood. Int J Cardiol 2019;274:303.
[5] Hsiu H, Jan MY, Lin Wang YY, Wang WK. Effects of aorta bending and renal ligation on the blood pressure: a simulation on arterial stiffening. Biomed Eng- App Bas C. 2003;15:243–8.
[6] Lin Wang YY, Wang WK. A hemodynamics model to study the collective behavior of the ventricular-arterial system. J Appl Phys 2013;113(2):024702.
[7] Young ST, Wang WK, Chang LS, Kuo TS. Specific frequency properties of renal and superior mesenteric arterial beds in rats. Cardiovasc Res 1989;23(6): 465–7.
[8] Young ST, Wang WK, Chang L, Kuo TS. The filter properties of the arterial beds of organs in rats. Acta Physiol Scand 1992;145(4):401–6.
[9] Chen CY, Wang WK, Kao T, Beverly CY, Chiang BC. Spectral analysis of radial pulse in patients with acute, uncomplicated myocardial infarction. Jpn Heart J 1993;34(2):131–43.
[10] Manisty C, Mayet J, Tapp RJ, Parker KH, Sever P, Poulter NR, et al. Wave reflection predicts cardiovascular events in hypertensive individuals independent of blood pressure and other cardiovascular risk factors: an ASCOT (Anglo-Scandinavian Cardiac Outcome Trial) Substudy. J Am Coll Cardiol 2010;56(1):24–30.
[11] Wang SH, Jan MY, Wang WK, Lin Wang YY. Effects of antihypertensive drugs on specific harmonic indices of the pulse waveform in normotensive Wistar Kyoto rats. Clin Exp Hypertens 2012;34(1):74–8.
[12] Weber T, O'Rourke MF, Lassnig E, Porodko M, Ammer M, Rammer M, et al. Pulse waveform characteristics predict cardiovascular events and mortality in patients undergoing coronary angiography. J Hypertens 2010;28:797–805.
[13] Wang SH, Hsu TL, Jan MY, Lin Wang YY, Wang WK. Age-related changes in specific harmonic indices of pressure pulse waveform. IFMBE Proceedings 2009;23:183–5.
[14] Chang CW, Liao KM, Chang YT, Wang SH, Chen YC, Wang GC. Fourth harmonic of radial pulse wave predicts adverse cardiac events in asymptomatic patients with type 2 diabetes. J Diabet Complicat 2019;33(6):413–6.
[15] Liao KM, Chang CW, Wang SH, Chang YT, Chen YC, Wang GC. 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. Phys Rep 2019;7(19):e14252.
[16] Liao KM, Chang CW, Wang SH, Chang YT, Chen YC, Wang GC. The first harmonic of radial pulse wave predicts major adverse cardiovascular and microvascular events in patients with type 2 diabetes. J Diabet Complicat 2019;33(11):107420.
[17] Chang CW, Wang WK. Reliability assessment for pulse wave measurement using artificial pulse generator. J Med Eng Technol 2015;39(3):177–84.
[18] National Health Insurance Administration. International Classification of Diseases, 10th Revision, ICD-10-CM/PCS in Clinical Classification of Diseases. Availabe from: https://www.nhi.gov.tw/Content_List.aspx?n=20443564F26622DC&topn=23C660CAACAA159D.
[19] Chen CY, Chang CW, Wang SH, Wang GC. Monitoring the hemodynamic status during three trimesters of pregnancy and non-pregnancy periods. Circ Res 2019;125(Suppl 1):A445.
[20] Soma-Pillay P, Nelson-Piercy C, Tolppanen H, Mebazaa A. Physiological changes in pregnancy. Cardiovasc J Afr 2016;27(2):89–94.
[21] O'Day MP. Cardio-respiratory physiological adaptation of pregnancy. Semin Perinatol 1997;21(4):268–75.
[22] Kristiansson P, Wang JX. Reproductive hormones and blood pressure during pregnancy. Hum Reprod 2001;16(1):13–7.
[23] Sanghavi M, Rutherford JD. Cardiovascular physiology of pregnancy. Circulation 2014;130(12):1003–8.
[24] Muto H, Yamamoto R, Ishii K, Kakubari R, Takaoka S, Mabuchi A, et al. Risk assessment of hypertensive disorders in pregnancy with maternal characteristics in early gestation: a single-center cohort study 2016;55(3):341–5.
[25] Pinto E. Blood pressure and ageing. Postgrad Med 2007;83(976):109–14.
[26] Campbell B, Davis SR, Abramson MJ, Mishra G, Handelsman DJ, Perret JL, et al. Menopause, lung function and obstructive lung disease outcomes: a systematic review. Climacteric 2018;21(1):3–12.
[27] van der Schouw YT, van der Graaf Y, Steyerberg EW, Eijkemans JC, Banga JD. Age at menopause as a risk factor for cardiovascular mortality. Lancet 1996;347(9003):714–8.
[28] Chotirmall SH. When Epidemiology meets Physiology: when epidemiology meets physiology: early menopause and associated respiratory risk. Ann Am Thorac Soc 2020;17(4):419–20.
[29] Wellons M, Ouyang P, Schreiner PJ, Herrington DM, Vaidya D. Early menopause predicts future coronary heart disease and stroke: the Multi-Ethnic Study of Atherosclerosis. Menopause 2012;19(10):1081–7.
[30] Muka T, Oliver-Williams C, Kunutsor S, Laven JSE, Fauser BCJM, Chowdhury R, et al. Association of age at onset of menopause and time since onset of menopause with cardiovascular outcomes, intermediate vascular traits, and all-cause mortality: a systematic review and meta-analysis. JAMA Cardiol 2016;1(7):767–76.
[31] Buford TW. Hypertension and aging. Ageing Res Rev 2016;26:96–111.
[32] Laurent S, Boutouyrie P. The structural factor of hypertension. Circ Res 2015;116(6):1007–21.
[33] Tikhonoff V, Casiglia E, Gasparotti F, Spinella P. The uncertain effect of menopause on blood pressure. J Hum Hypertens 2019;33(6):421–8.
[34] Maas AH, Franke HR. Women's health in menopause with a focus on hypertension. Neth Heart J 2009;17(2):68–72.
[35] Chen CY, Chang CW, Chang YT, Wang SH, Wang GC. The effects of age, menopause, and body mass index on blood pressure and radial pulse wave in women. Circ Res 2019;125(Suppl 1):A176.
[36] White RE. Estrogen and vascular function. Vasc Pharmacol 2002;38(2):73–80.
[37] Lin Wang YY. 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.
[38] Lin Wang YY, Hsu TL, Jan MY, Wang WK. Review: theory and applications of the harmonic analysis of arterial pressure pulse waves. J Med Biol Eng 2010;30(3):125–31.