Cardiology in the Young

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Use of phase-contrast MRI to measure aortic stiffness in young-onset hypertension: a pilot study

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Abstract

Background: Young-onset hypertension is defined as hypertension diagnosed before the age of 40 years. Aortic pulse wave velocity is an indication of aortic stiffness. MRI assessment has been well verified compared to invasive pressure recordings for evaluating aortic pulse wave velocity. In this study, we aimed to determine whether aortic stiffness played a role in the aetiology of young-onset hypertension by calculating pulse wave velocity using MRI. *Methods:* We enrolled 20 patients diagnosed with young-onset hypertension and 20 volunteers without hypertension. Aortic pulse wave velocity was measured by cardiac MRI and protocol for the pulse wave velocity measurement involved the use of a 1.5 T scanner to acquire velocity-encoded, phase-contrast transverse aortic cine images. Sagittal oblique images used to measure the distance (ΔX) between the ascending aorta and descending aorta for the calculation of pulse wave velocity. The aortic flow versus time curves of ascending aorta and descending aorta were automatically obtained from the phase-contrast MRI images. Using these curves, the temporal shift (ΔT) was measured by Segment Medviso. *Findings:* The mean pulse wave velocity was 8.72 (SD 2.34) m/second (range: 7–12.8 m/second) for the patient group and 5.96 (standard deviation 1.86) m/second (range: 4.8–7.1 m/second) for the control group. The pulse wave velocity values were significantly higher in the patient group compared to the control group ($p < 0.001$). *Interpretation:* Aortic stiffness may play a role in the aetiology of young-onset hypertension and serve as a non-invasive and reliable screening tool when measured by MRI.

Young-onset hypertension is defined as hypertension diagnosed before the age of 40 years, and it is rare. Young-onset hypertension cases present with essential hypertension characterised by peripheral vascular resistance.[1,2] Arterial stiffness is closely associated with atherosclerosis and contributes to vascular diseases through endothelial dysfunction and stretching of the vessels. Aortic pulse wave velocity is an indication of aortic stiffness.[3–5] Pulse wave velocity is defined as the rate at which the pressure wave flows through a vessel part.[6] Pulse wave velocity measurement is generally considered as a simple, non-invasive, reliable, and reproducible method for determining arterial stiffness. Pulse wave velocity is a strong indicator of future cardiovascular events and all-cause mortality.[7]

The measurement of pulse wave velocity offers an opportunity to identify patients at risk and make timely interventions, such as lifestyle changes and medication therapy. Unlike conventional cardiovascular risk factors, pulse wave velocity is a stable parameter that gradually becomes abnormal and represents vascular ageing.[8] It has been proposed as an independent parameter for the evaluation of individual risk.[9,10]

Several techniques, both invasive and non-invasive, are currently used to assess arterial stiffness. As non-invasive methods, arterial tonometry and ultrasound and MRI-assessed pulse wave velocity measurement are commonly used for the estimation of aortic stiffness.[11–15] These techniques indirectly measure the arterial stiffness of the entire aorta.[12,15] The pulse wave velocity measurement using the arterial tonometer is based on the principle of reflectance of the peripheral pulse pressure, but it does not only focus on the compliance of the thoracic aorta but also reflects the wall characteristics of both the abdominal aorta and the carotid and femoral arteries.[15–17]

MRI-assessed pulse wave velocity measurement is based on the measurement of the flow wave in the analysis planes. Unlike other methods, such as tonometry and ultrasound, which are frequently used in clinical trials, MRI assessment is very suitable for evaluating aortic stiffness by focusing on the thoracic aorta, regardless of its geometric shape.[17,18] In addition, this method has been well verified compared to invasive pressure recordings.[19]

In this study, we aimed to determine whether aortic stiffness played a role in the aetiology of young-onset hypertension by calculating pulse wave velocity using MRI.

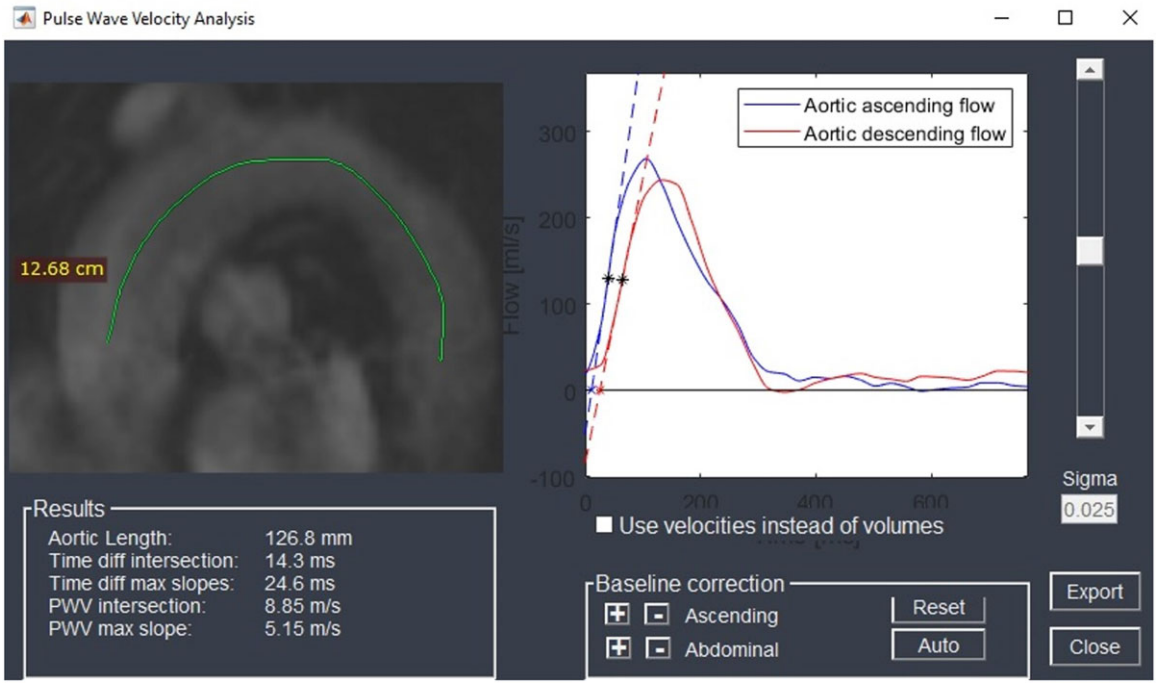

Figure 1. Segment (Medviso) inter face.

Methods

Patients

Between February, 2018 and September, 2019, 20 patients newly diagnosed with young-onset hypertension (patient group) and 20 volunteers (control group) without hypertension (all aged <40 years) were included in the study. The volunteers included in the control group were similar in age, gender, and body mass index to the patient group. Individuals aged over 18 and under 40 years without any other chronic disease other than hypertension and no history of drug use were included in the patient group. Patients with a rheumatologic disease, hyperlipidaemia, or any acute or chronic disease were excluded. Three blood pressure measurements were made in office, with the patient at rest seated for at least 10 minutes. Renal artery doppler USG was performed in all patients to rule out secondary hypertension. All patients underwent adrenal gland evaluation during MRI examination, in which adrenal pathologies were excluded. All patients underwent MR imaging within a maximum of one year from the time of diagnosis. To evaluate aortic stiffness, phase-contrast images were obtained by MRI for the aortic flow in all patients and the volunteers in the control group. Written consent was received from all participants. The study was approved by the local medical ethics committee and was conducted according to the principles in the Declaration of Helsinki.

MRI evaluation of aortic stiffness

The MRI protocol for the pulse wave velocity measurement involved the use of a 1.5 T scanner (Siemens, Erlangen, Germany) to acquire two consecutive non-breath-held, through-plane, velocity-encoded, phase-contrast transverse aortic cine images, one from the aortic arch at the level of pulmonary artery and the other 2 cm above the aortic bifurcation. Image analysis was performed offline by the same analyst blinded to the identity of the patients.

Manual contour drawing for the calculation of pulse wave velocity (the length (Δx) between ascending aorta and descending aorta was measured as indicated by the line) in the aorta. Pulse wave velocity was calculated using the time-to-foot approach implemented through the freely available software Segment cardiac MRI (Medviso, publicly available at https://medviso.com/). For quantitative flow curves, automatic vessel segmentation was performed with manual corrections where needed. Delineations were performed in magnitude images and guided by phase-contrast images where appropriate. Specifically, carotid pulse wave velocity was calculated as x/t (expressed in m/s), where x is the aortic path length between the carotid arch, and t is the time delay between the arrival of the foot of the pulse wave at these locations. Pulse wave velocity estimates were obtained by two independent raters and averaged to generate the final pulse wave velocity values(Fig 1). In our group, the mean aortic arch length was 17.6 ± 3.2 cm. The inter-rater correlation of pulse wave velocity estimates is 0.88, with an r2 of 0.70.

Statistical analysis

All data were analysed using the Statistical Package for Social Sciences (SPSS Inc., version 21.0, Chicago, IL, USA). The normally distributed data were expressed in mean and standard deviation, while the data without normal distribution were given as median (25–75%) values. The comparison of the categorical and continuous variables was performed using the chi-square and Mann–Whitney *U* tests, respectively.

Results

Twelve of the patients with young-onset hypertension were male and eight were female. The mean age of our young-onset hypertension group was 29.9 (18–40) years. All patients underwent MR imaging within a maximum of one year from the time of

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Table 1. Demographic features of the patients with young-onset hypertension and the control group

	Patients (n = 20)	Controls (n = 20)	p value
Age (mean and SD)	29.9 (SD 8.5)	30.8 (SD 5.9)	0.642
Gender (male)	12 (60%)	11(55%)	0.469
Body mass index (kg/m^2)	26.03 (SD 3.51)	25.6 (SD 4.36)	0.094
Blood pressure (systolic/diastolic, mmHg)	148.44/97.50	108.38/75.63	<0.001
LDL (mg/dl)	96.5 (SD 16.7)	94.7 (SD 14.3)	0.134
Triglyceride (mg/dl)	178.6 (SD 19.2)	176 (SD 15.7)	0.093

SD: standard deviation; LDL: low-density lipoprotein.

Table 2. MRI-assessed PWV measurements of the patient and control groups.

	Patients	Controls	p value
ΔT (mean)	19.28	26.52	<0.005
ΔX (mean)	15.8	15.5	0.023
MR PWV	8.72 (SD 2.34)	5.96 (SD 1.86)	<0.001

diagnosis. The mean time between MR imaging and diagnosis was calculated as 25.3 (3–45 days). Of the 20 individuals in the control group, 11 were male and nine were female, with a mean age of 30.8 years (range: 18–39 years). The body mass index was 26.03 (standard deviation 3.51) kg/m^2 for the patient group and 25.6 (standard deviation 4.36) kg/m^2 for the control group. There was no significant difference between the patient and control groups in terms of age, gender, and body mass index. In the patient group, the mean low-density lipoprotein was 96.5 (standard deviation 16.7) mg/dl and triglyceride was 178.6 (standard deviation 19.2). The mean low-density lipoprotein and triglyceride values of the control group were 94.7 (standard deviation 14.3) and 176 (standard deviation 15.7), respectively.

There was no significant difference between the patient and control groups in terms of the low-density lipoprotein and triglyceride values. The mean blood pressure was 148/97 mmHg in the patient group and 108.38/75.63 mmHg in the control group (Table 1). The mean pulse wave velocity was 8.72 (standard deviation 2.34) m/second (range: 7–12.8 m/second) for the patient group and 5.96 (standard deviation 1.86) m/second (range: 4.8–7.1 m/second) for the control group. The pulse wave velocity values were significantly higher in the patient group compared to the control group ($p < 0.001$) (Table 2).

Discussion

Hypertension is the most common chronic disease and is one of the major causes of heart failure, stroke, and chronic renal failure. The earlier the onset of hypertension, the longer the exposure time, resulting in a greater risk for cardiovascular events. Although there is not sufficient information about the pathogenesis of young-onset hypertension in the literature, it has been suggested that the main underlying haemodynamic abnormality may be increased peripheral vascular resistance, which causes vascular remodelling in the arteries. Increased arterial stiffness is an important parameter to determine the cardiovascular risk.[20–22]

In addition to increased aortic stiffness being determined by pulse wave velocity measurement, it has been shown in the literature that there is a relationship between aortic stiffness measured by pulse wave velocity and age, ethnicity, and future CVDs.[23–26] In a meta-analysis, a 1 m/second increase in pulse wave velocity was reported to be associated with an 11% increase in cardiovascular death.[27] Pulse wave velocity is an indirect measure of arterial stiffness, and many studies have measured pulse wave velocity using different methods, such as Doppler ultrasonography and tonometry.[28,29] The most accurate evaluation of aortic pulse wave velocity can be performed by the measurement of intra-arterial pressure. However, this is an invasive modality, and therefore not suitable for widespread clinical use.[30,31]

Tonometry and ultrasound are more commonly used in pulse wave velocity measurement. However, both modalities only provide an estimate of aortic pulse wave velocity due to inadequate acoustic windows and insufficient spatial resolution along the length of the aorta.[32,33] Pulse wave velocity measurement using MRI is widely used as a non-invasive and reliable technique. The most common method of measuring aortic pulse wave velocity is to calculate the aortic length and transit time, i.e., the time it takes for the systolic wave to travel from one reference point within the aorta to another.[34–36]

MRI allows for an accurate evaluation of the blood flow rate with sufficient temporal and spatial resolution to investigate the travelling of the aortic systolic flow wave. The true path length of the pulse wave along the aorta can be directly assessed by MRI even in cases of aortic tortuosity, and the regional elastic properties of the aorta can be examined depending on the number of aortic segments studied.[30,37–39]

The presence and severity of hypertension is known to accelerate the increase in aortic pulse wave velocity.[40] In a 6-year study measuring aortic stiffness as carotid-femoral pulse wave velocity, the presence of hypertension was found to be associated with progression of aortic stiffness compared to normotensive subjects.[41] Similarly, in our previous tonometry study conducted with young-hypertension cases, we found pulse wave velocity to be significantly higher in patients with hypertension.[42]

Ohyama et al, who followed up hypertension cases of multi-ethnic origin aged 45 years or over for 10 years, measured their aortic stiffness by MRI and reported that blood pressure control was effective in stopping the progression of aortic stiffness.[43] Van Elderen et al evaluated type I diabetics with normal renal functions in terms of their pulse wave velocity values measured on MRI and found that this patient group had increased pulse wave velocity, independent of renal dysfunction.[44] Similarly, other researchers showed that the pulse wave velocity increase measured by MRI in patients with type I diabetes was associated with cardiac dysfunction and cerebral small vessel disease.[45]

In another study, the pulse wave velocity measurements were undertaken by MRI in end-stage renal disease cases with decreased

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arterial compliance and were found to be significantly higher compared to the control group.[46]

In the current study, the pulse wave velocity values calculated by MRI were found to be increased in hypertensive patients compared to the control group, which is in agreement with the literature. To the best of our knowledge, in the literature, aortic stiffness has not been previously investigated with MRI in patients with young-onset hypertension. Our findings suggest that increased arterial stiffness may also contribute to the aetiology of hypertension that begins at a young age.

The sample size was relatively small, and larger studies are needed to confirm the clinical role of aortic stiffness in cardiovascular risk classification and treatment optimisation. There is also a need for further studies comparing aortic stiffness measured by MRI with other methods.

In conclusion, aortic stiffness may play a role in the aetiology of young-onset hypertension and serve as a non-invasive and reliable screening tool when measured by MRI.

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Authors' contributions. C.O.G. and E.D. designed the study. C.O.G and S.G. investigated and supervised the findings of this work. S.S. verified the mathematical methods. All authors discussed the results and contributed to the final manuscript.

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Conflicts of interest. None.

Ethical standards. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national guidelines on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008, and has been approved by the institutional committees (AFSU ethical commitee).

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