Ultrasound Imaging Pulse Wave Velocity Technology Assessment of the Impact of Hypertension and Hyperglycemia on Carotid Artery Stiffness

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Abstract: Hypertension and diabetes are two common chronic diseases that contribute to arterial stiffness. To evaluate the differential impacts of hypertension and hyperglycemia on carotid artery stiffness, this study conducted a retrospective analysis of ultrasound imaging pulse wave parameters in cases diagnosed with primary hypertension, Type II diabetes, and normal health check-ups at our hospital. The results showed that the one-way ANOVA did not reveal significant statistical differences among the groups overall. However, post-hoc multiple comparison tests indicated that there was a statistical difference in the pulse wave parameter L-CCA PWV-BS between hypertensive patients and the normal group. Additionally, the pulse wave parameter L-CCA PWV-ES showed statistical differences between the hypertensive patients and the normal group, as well as between the people with diabetes and the normal individuals. The pulse wave parameter R-CCA PWV-BS showed a statistical difference between the people with diabetes and normal individuals, while R-CCA PWV-ES showed statistical differences between the hypertension and the diabetes patient groups, as well as between the hypertensive patients and the normal group. Consequently, this study found that between two chronic diseases, hypertension is the one most likely to cause stiffness in the carotid artery.

Keywords: Hypertension; Diabetes; Arteriosclerosis; Ultrasound; Pulse Wave

1. Introduction

Atherosclerosis in large arteries is one of the most dangerous signals for cardiovascular diseases, thus detecting the elasticity of large arteries provides important evidence for the timely detection, diagnosis, and management of cardiovascular diseases [1]. It is generally believed that hypertension and hyperglycemia strongly promote arteriosclerosis.

Arterial elasticity is one of the key indicators reflecting the arterial diastolic function and compliance. The pathological process of reduced arterial elasticity is primarily manifested by increased stiffness of the arterial wall and thickening of the vessel wall, leading to an elevated velocity of blood flow through the lumen.

There are various methods to assess the elasticity of large arteries, among which pulse wave velocity (PWV) refers to the propagation speed of the pulse wave between two predetermined points in the arterial system. The measurement of PWV can effectively evaluate the expansibility and stiffness of the arterial wall.

Ultrafast ultrasound imaging pulse wave velocity (uf-PWV) leverages advanced imaging technology to capture the real-time motion trajectory of the intima-media layer in the common carotid artery. This enables precise measurement of pulse wave velocity, which offers insights into the elasticity of the common carotid artery. It is a convenient, rapid ultrasound imaging technique that is economical, simple, non-invasive, and highly reproducible [2].

This study aims to use uf-PWV technology to measure the carotid PWV parameters of all research samples to assess their arterial stiffness. By comparing the differences in carotid ultrafast pulse wave velocity among the hypertensive, diabetic, and normal groups, we evaluate the impact of hypertension and hyperglycemia on arterial stiffness.

2. Materials and Methods

2.1 General Information

A retrospective analysis was conducted on cases diagnosed with primary hypertension, type II diabetes, and normal volunteers at our hospital from September 19, 2017, to October 21, 2019.

Inclusion criteria for the hypertension group: The hypertension cases in this study met the diagnostic criteria of the "2010 Chinese Hypertension Prevention and Treatment Guidelines."

Exclusion criteria for the hypertension group:
(1) Patients with arterial occlusion.
(2) Patients with secondary hypertension.
(3) Patients with a clear history of coronary artery disease or stroke, or those who were diagnosed based on previous auxiliary examination findings.
(4) Patients with cardiopulmonary disease, hyperlipidemia, or chronic kidney disease.
(5) Patients with primary hyperthyroidism.
(6) Patients who smoked, engaged in intense exercise, or consumed coffee before the examination.
(7) Patients with unstable measurement data, those unable to obtain PWV parameters, or those with data errors outside the specified range.

Inclusion criteria for the diabetes group: The diabetes cases in this study met the diagnostic criteria of the Chinese Diabetes Association, namely: in the absence of clear hyperglycemia.

Exclusion criteria for the diabetes group:
(1) Patients with severe anemia, hyperthyroidism, liver cirrhosis, asthma, or major systemic diseases such as malignant tumors.
(2) Patients with cardiovascular or cerebrovascular conditions.
(3) Patients with autoimmune diseases.
(4) Patients with unstable measurement data, those unable to obtain PWV parameters, or those with data errors outside the specified range.
(5) Patients who smoked, engaged in intense exercise, or consumed coffee before the examination.

Inclusion criteria for the normal control group: Volunteers without underlying diseases and with normal blood pressure, serum biochemical Indices, and body mass index, who voluntarily participated in the experiment.

Exclusion criteria for the healthy control group:
(1) Those who withdrew from the study.
(2) Those with unstable parameter measurement data or data errors outside the specified range.

This study was approved by the hospital's ethics committee, and all participants signed informed consent forms to protect patient privacy and voluntarily participated in this study.

This study was approved by the hospital's research ethics committee, and all participants provided written informed consent to protect their privacy and voluntarily take part in the investigation.

2.2 Methods

2.2.1 Measurement of carotid uf-PWV

Instrument: The study utilized the Super Sonic Aixplorer ultrasound diagnostic system (France), equipped with the SL15-4 probe, operating at a frequency range of 4-15 MHz, and employing the Carotid preset. The device features color Doppler and automated intima-media thickness (IMT) measurement capabilities.

The ultrafast imaging technology was used to assess the carotid artery pulse wave velocity at the start of systole (PWV-BS) and the end of systole (PWV-ES) in the study participants.

Procedure: Patients were placed in a supine position and asked to breathe calmly, exposing both sides of the neck. B-Mode was selected, and the measurement area was taken at 1.0-1.5 cm below the carotid sinus, with the carotid artery scanned from the side of the neck. The scanning plane was away from the carotid bifurcation and plaque formation area, passing through the maximum diameter of the artery lumen. The probe was appropriately pressed so that the vessel wall was parallel to the probe surface, with the intima-media clearly displayed, and efforts were made to avoid artifacts from the thyroid, muscles, and vessel wall in the lumen. On the touch screen, the PWV function was selected, and the patient was instructed to remain still while the probe was held steady for a 2-second acquisition period. If the acquisition was unsatisfactory, the sample frame size and position were adjusted to select the vascular segment, making the sample frame as large as possible to include more information. The Select button on the control panel was then clicked, which displayed the velocity-time color map of the anterior and posterior wall movements of the artery. The system automatically calculated and displayed the pulse wave velocity at the start of systole (PWV-BS) and the end of systole (PWV-ES), with the Δ± value (representing the standard deviation) controlled within 10% of the PWV-BS or PWV-ES value, indicating good data stability. Measurements were repeated three times, as shown in Figure 1.

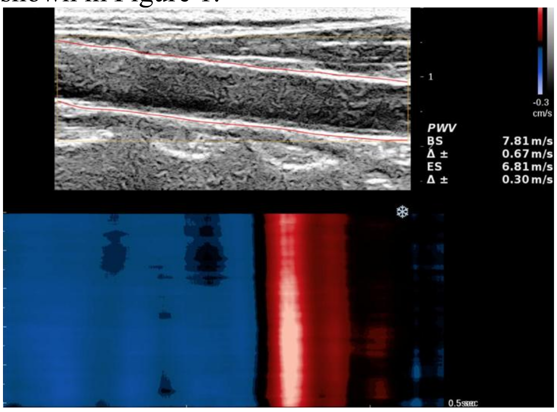

Figure 1. PWV Automatic Data Collection Process

2.2.2 Laboratory tests

Venous blood samples were collected from the study participants after an overnight fast. An automated biochemical analyzer was used to measure the following parameters from the blood samples: fasting blood glucose, 1-hour postprandial blood glucose, 2-hour postprandial blood glucose, glycated hemoglobin, lipoprotein (a), triglycerides, total cholesterol, high-density lipoprotein, low-density lipoprotein, apolipoprotein A1, and apolipoprotein B, as well as other plasma biochemical indicators.

2.2.3 Statistical analysis

The data were statistically analyzed using SPSS Version 25.0 software (IBM, USA). Measurement data were expressed as mean ± standard deviation ($\bar{x} \pm s$). One-way ANOVA was used to analyze the statistical differences in the four carotid pulse wave parameters (bilateral PWV-BS and bilateral PWV-ES) among the hypertension group, diabetes group, and normal control group, to investigate the impact of hypertension and diabetes as risk factors on arterial stiffness. A p-value < 0.05 was considered statistically significant. Post hoc multiple comparisons were then performed to analyze the specific statistical differences between groups, with a p-value < 0.05 indicating a significant difference between the groups.

3. Results

A total of 251 participants were recruited, including 138 males and 113 females, with a male-to-female ratio of 1.2:1. The age range was 20 to 83 years, with a mean age of 49.94 ± 13.89 years. Of the total, 129 individuals were in the hypertension group, including 81 males and 48 females, with a male-to-female ratio of 1.7:1. Their age range was 22-83 years, with a mean age of 58.32 ± 11.00 years. The diabetes group consisted of 61 participants, 33 men and 28 women, with a male-to-female ratio of 1.2:1. The age range was 40-68 years, with a mean age of 54.27 ± 8.51 years. The normal control group included 61 individuals, 29 males and 32 females, with a male-to-female ratio of 29:32. Their age range was 20 to 70 years, with a mean age of 40.64 ± 11.34 years.

In the hypertension group, the average values of PWV-BS and PWV-ES in the right common carotid artery were 5.82 ± 1.25 m/s and 8.18 ± 2.26 m/s, respectively. The average values of PWV-BS and PWV-ES in the left common carotid artery were 5.67 ± 1.27 m/s and 8.36 ± 2.10 m/s, respectively. In the diabetes group, the mean values of PWV-BS and PWV-ES in the right common carotid artery were 5.11 ± 0.85 m/s and 6.27 ± 1.89 m/s, respectively. The mean values of PWV-BS and PWV-ES in the left common carotid artery were 5.30 ± 1.31 m/s and 7.64 ± 1.46 m/s, respectively. In the normal control group, the average values of PWV-BS and PWV-ES in the right common carotid artery were 5.90 ± 1.20 m/s and 6.93 ± 1.78 m/s, respectively. The average values of PWV-BS and PWV-ES in the left common carotid artery were 5.16 ± 1.22 m/s and 6.12 ± 1.34 m/s, respectively. See Table 1 for details.

The one-way ANOVA test showed no significant statistical differences between populations. The results of the homogeneity of variance test showed that the p-values for the L-CCA PWV-BS parameter and R-CCA PWV-BS parameter were both greater than 0.05. The significance test p-values for L-CCA PWV-ES parameters and R-CCA PWV-ES parameters are both less than 0.05, as shown in

Table 2. One way ANOVA test results: No statistical difference was found in the tests of parameters L-CCA PWV-BS and R-CCA PWV-BS, with a p-value greater than 0.05. The p-values for the significance tests of L-CCA PWV-ES and R-CCA PWV-ES parameters were both less than 0.05, as shown in Table 3.

Table 1. General Descriptive Statistics Homogeneity of Variance Test

		Mean	Standard deviation	Minimum	Maximum
LCCA PWV-BS	Hypertension group	5.67	1.27	3.11	8.50
	Diabetes group	5.30	1.31	3.40	7.87
	Normal control group	5.16	1.22	3.31	8.27
	Total	5.41	1.26	3.11	8.50
LCCA PWV-ES	Hypertension group	8.36	2.10	3.22	12.48
	Diabetes group	7.64	1.46	5.23	9.96
	Normal control group	6.12	1.34	3.41	9.64
	Total	7.28	2.04	3.22	12.48
RCCA PWV-BS	Hypertension group	5.82	1.25	3.68	8.73
	Diabetes group	5.11	0.85	4.00	6.40
	Normal control group	5.89	1.20	3.99	9.45
	Total	5.79	1.21	3.68	9.45
RCCA PWV-ES	Hypertension group	8.18	2.26	3.18	13.25
	Diabetes group	6.27	1.89	3.72	9.50
	Normal control group	6.93	1.78	4.16	12.58
	Total	7.45	2.12	3.18	13.25

Table 2. Homogeneity of Variance Test

		Levin statistics	Significance
L-CCA PWV-BS	Based on mean	0.007	0.993
	Based on median	0.007	0.993
	Adjusted degrees of freedom based on median	0.007	0.993
	Based on the average value after pruning	0.003	0.997
L-CCA PWV-ES	Based on mean	8.947	0.000
	Based on median	8.021	0.001
	Adjusted degrees of freedom based on median	8.021	0.001
	Based on the average value after pruning	8.991	0.000
R-CCA PWV-BS	Based on mean	1.006	0.368
	Based on median	1.011	0.367
	Adjusted degrees of freedom based on median	1.011	0.367
	Based on the average value after pruning	1.018	0.364
R-CCA PWV-ES	Based on mean	3.177	0.045
	Based on median	3.180	0.045
	Adjusted degrees of freedom based on median	3.180	0.045
	Based on the average value after pruning	3.338	0.039

Table 3. One-way ANOVA

		Square sum	Mean square	F	Significance
L-CCA PWV-BS	Inter group	8.142	4.071	2.607	.078
	Intra group	204.532	1.561		
	Total	212.674			
L-CCA PWV-ES	Inter group	155.184	77.592	25.562	.000
	Intra group	397.646	3.035		
	Total	552.830			
R-CCA PWV-BS	Inter group	5.816	2.908	2.025	.136
	Intra group	188.142	1.436		
	Total	193.958			
R-CCA PWV-ES	Inter group	64.176	32.088	7.842	.001
	Intra group	536.046	4.092		
	Total	600.221			

Post hoc multiple comparison LSD results (Table 4) showed the following: For the pulse wave parameter L-CCA PWV-BS, there was a statistically significant difference between the hypertension group and the normal control group, with a p-value less than 0.05. For the pulse wave parameter L-CCA PWV-ES, statistically significant differences were found between the hypertension group and the normal control group, and between the diabetes group and the normal control group, with p-values less than 0.05.For the pulse wave parameter R-CCA PWV-BS, there was a statistically significant difference between the diabetes group and the normal control group, with a p-value less than 0.05.For the pulse wave parameter R-CCA PWV-ES, statistically significant differences were found between the hypertension group and the diabetes group, and between the hypertension group and the normal control group, with p-values less than 0.05.

Table 4. Statistical Analysis Results of Post Hoc Multiple Comparison LSD Method

dependent variable	(I) Group	(J) Group	Mean value difference (I-J)	standard deviation	Significance	95% confidence interval	
						Min	Max
L-CCA PWV-BS	1	2	0.36271	0.40880	0.377	-0.4460	1.1714
		3	0.51076*	0.22534	0.025	0.0650	0.9565
	2	1	-0.36271	0.40880	0.377	-1.1714	0.4460
		3	0.14804	0.40931	0.718	-0.6617	0.9578
	3	1	-0.51076*	0.22534	0.025	-0.9565	-0.0650
		2	-0.14804	0.40931	0.718	-0.9578	0.6617
L-CCA PWV-ES	1	2	0.71506	0.57001	.212	-0.4126	1.8427
		3	2.23520*	0.31420	.000	1.6136	2.8568
	2	1	-0.71506	0.57001	.212	-1.8427	0.4126
		3	1.52014*	0.57071	0.009	0.3911	2.6492
	3	1	-2.23520*	0.31420	0.000	-2.8568	-1.6136
		2	-1.52014*	0.57071	0.009	-2.6492	-0.3911
R-CCA PWV-BS	1	2	0.70720	0.39208	0.074	-0.0684	1.4828
		3	-0.07896	0.21612	0.715	-0.5065	0.3486
	2	1	-0.70720	0.39208	0.074	-1.4828	0.0684
		3	-0.78615*	0.39257	0.047	-1.5627	-0.0096
	3	1	0.07896	0.21612	0.715	-0.3486	0.5065
		2	0.78615*	0.39257	0.047	0.0096	1.5627
R-CCA PWV-ES	1	2	1.90565*	0.66181	0.005	0.5964	3.2149
		3	1.24122*	0.36480	0.001	0.5196	1.9629
	2	1	-1.90565*	0.66181	0.005	-3.2149	-0.5964
		3	-0.66443	0.66263	0.318	-1.9753	0.6464
	3	1	-1.24122*	0.36480	0.001	-1.9629	-0.5196
		2	0.66443	0.66263	0.318	-0.6464	1.9753

The comprehensive analysis results showed that for the bilateral carotid PWV-ES parameters, the values for the hypertension group were greater than those for the diabetes group, which were greater than those for the normal control group, with statistical differences among the groups. For the left carotid PWV-BS parameter, the hypertension group had higher values than the normal control group, with a statistical difference. For the right carotid PWV-BS parameter, the diabetes group had higher values than the normal control group, with a statistical difference. In summary, based on the impact on carotid artery stiffness, the severity of the risks is ranked as follows: hypertension > diabetes > normal.

4. Discussion

Hypertension and diabetes, two common chronic diseases, are associated with cardiovascular events such as coronary heart disease and stroke. Compared to normal individuals, those with high normal blood pressure have a four times higher chance of developing hypertension. Atherosclerotic cardio cerebrovascular disease is a chronic progressive disease, vascular atherosclerosis is the pathological basis, hypertension, hyperlipidemia, hyperglycemia and other factors are the main causes of atherosclerosis. The measurement of pulse wave velocity can be effectively used to evaluate arterial wall dilation and stiffness.

According to the 2013 European Guidelines for the Prevention and Treatment of Hypertension, cervical femoral pulse wave velocity (Cf-PWV) is an important non-invasive, simple, economical, and effective method for assessing risk factors for arteriosclerosis and cardiovascular disease. The "2010 Guidelines for the Prevention and Treatment of Hypertension in China" also consider PWV an important evaluation indicator for target organ damage.

Uf-PWV wave technology is a newly developed method that can be applied to measure arterial PWV. It has the advantages of accurate measurement, convenient operation, short acquisition time, good compliance of the examinee, and significantly shortens the examination time. Research [3] suggests that high-speed imaging technology can quickly measure carotid artery PWV, providing a convenient tool for early and accurate reflection of vascular elasticity changes in clinical practice. Qiu Lanyan et al. found that rapid imaging technology can effectively reflect the arterial elasticity status of the subject by quantitatively analyzing the values of BS and ES [4]. Furthermore, Xu Yijun et al. [5] found that the uf-PWV imaging technology is a new technique for detecting PWV, and the parameters obtained can effectively reflect the changes in carotid artery elasticity function in patients with primary hypertension. Research [6] has shown that high-speed ultrasound imaging is an effective and convenient method for directly measuring PWV in the common carotid artery region of hypertensive patients.

Additionally, experiments on vascular wall morphology and function in the early stage of atherosclerosis have found that PWV can be used to predict the morphological changes of the arterial wall at an earlier stage, and its potential predictive value is also very prominent in the early diagnosis of atherosclerosis, as arterial stiffness increases and PWV forward wave velocity increases [7-8].

Research has consistently demonstrated that PWV is an independent predictor of stroke risk. A large-scale, prospective longitudinal study of hypertensive patients further confirmed that PWV is an independent risk factor for stroke [9]. A study by Hajjar et al. [10] found that reducing PWV has the potential to be a therapeutic target for preventing cognitive impairment and dementia.

PWV is used for monitoring early renal damage in hypertension. The pathological basis of hypertensive renal damage is mainly renal arteriolar sclerosis, and hypertension lasting 5-10 years can lead to renal arteriolar sclerosis, narrowing of the lumen and thickening of the wall, resulting in arteriolar renal sclerosis [11]. Research [12] has found that the urinary microalbumin/creatinine ratio in hypertensive patients is positively correlated with an increase in brachial-ankle pulse wave velocity (ba-PWV), indicating a close correlation between an increase in urinary microalbumin and a decrease in arterial elasticity. This suggests that deteriorating vascular function, as reflected by elevated PWV, is associated with early signs of kidney damage in hypertensive individuals.

Furthermore, a 2017 CATOD study proposed a specific correlation between arterial stiffness in different locations and target organ damage in hypertension [13]. In this study, patients with primary hypertension underwent both cf-PWV and carotid PWV measurements. The analysis showed that an increase in cf-PWV, a measure of central arterial stiffness, was associated with renal target organ damage, while an increase in carotid PWV was associated with left ventricular hypertrophy. This indicates that regional differences in arterial stiffening can have distinct impacts on end-organ complications in hypertension.

PWV has emerged as a valuable tool for predicting early cardiovascular disease risk in hypertensive patients. A study of 251 patients undergoing coronary angiography found that brachial-ankle PWV (ba-PWV) and ankle-brachial index (ABI) have significant value in the early identification and monitoring of coronary artery disease progression [14]. Further observations suggest that ABI, PWV, and carotid c-IMT are correlated with the degree of coronary artery stenosis, allowing identification of asymptomatic individuals at higher risk of future cardiovascular events [15]. Research has also shown that increased ba-PWV is associated with a higher risk of developing cerebral infarction [16-17]. While ba-PWV can be used to assess vascular elasticity before moderate stenosis, it has limited diagnostic utility for severe stenosis and occlusion, though it remains a useful indicator of lower limb arterial stiffness [18]. Additionally, studies indicate ba-PWV is closely related to early morning hypertension and lower limb atherosclerosis, serving as an effective marker of early arterial stiffening in these conditions [19]. Finally, the ba-PWV value has been found to correlate well with the degree of hypertensive retinal lesions, suggesting it can reflect the impact of elevated blood pressure on the microvasculature [20].

Previous studies have indicated that high blood sugar levels can readily lead to increased arterial stiffness, as measured by PWV. A longitudinal study of 417 diabetic patients found that elevated glycated hemoglobin levels were positively correlated with cf-PWV over a 4.2-year follow-up period [21]. Similarly, other research has shown that fasting blood glucose and glycosylated hemoglobin concentrations are positively associated with cf-PWV, with the latter being an important independent predictor of central arterial stiffness [22].

The increased cardiovascular and stroke risk associated with metabolic syndrome is well-established. According to Chinese hypertension guidelines, patients with metabolic syndrome have a 10-fold higher 10-year cardiovascular disease risk and 2-3 times higher ischemic and hemorrhagic stroke risk compared to those without metabolic abnormalities [23].

A large cross-sectional study involving over 20,000 subjects across Europe and the US found that the presence of various metabolic abnormality combinations, including hypertriglyceridemia, hyperglycemia, elevated blood pressure, and abdominal obesity, was associated with higher cf-PWV relative to normal controls [24]. The groups with the most pronounced increases in central arterial stiffness were those with multiple metabolic disturbances. Notably, a recent study observed that cf-PWV values increase as the number of abnormal metabolic components increases [25]. In summary, these findings highlight the strong link between dysregulated glucose and lipid metabolism, as seen in metabolic syndrome, and increased arterial stiffness, which is an important predictor of cardiovascular complications.

Previous literature believed that the measurement of PWV-ES parameters using carotid uf-PWV is a new method for the early diagnosis and quantitative assessment of arterial stiffness and atherosclerosis risk [26]. This view is broadly consistent with the findings of the current study.

The study found that the order of impact on carotid artery PWV-ES parameters is: hypertension > hyperglycemia > normal conditions. There is a notable difference in the degree of arterial stiffness caused by hypertension and hyperglycemia, with hypertension exerting a significantly stronger effect on carotid artery stiffness compared to hyperglycemia. Based on the literature, the authors suggest that this phenomenon is attributable to the distinct pathophysiological mechanisms by which these conditions induce arterial stiffening.

Hyperglycemia primarily leads to arteriosclerosis through two key mechanisms. Firstly, the elevation in blood sugar levels reduces the bioavailability of nitric oxide, increases oxidative stress, triggers subclinical chronic inflammation, induces sympathetic tension, and alters the structure or composition of elastin and collagen fibers in the vascular wall, collectively resulting in pathological changes in the vascular bed. [27] Secondly, the differentiation and proliferation of vascular smooth muscle cells affect the structure of the vascular wall, ultimately leading to increased arterial stiffness. [28] Additionally, advanced glycation end products also play a significant role in the process of atherosclerosis, causing changes in the molecular structure within the vascular wall. [29]

In contrast, when hypertension causes arteriosclerosis, the increase in arterial blood pressure leads to vascular damage and accelerates the occurrence of atherosclerosis. Chronic hypertension affects the intima of blood vessels, damages the endothelium, promotes lipid deposition, and increases the number and thickness of smooth muscle cells, collagen fibers, and elastic fibers, all of which contribute to the development of atherosclerosis.

Therefore, the research findings of the present study are generally consistent with previous reports.

This study is a single-center retrospective investigation, and the sample size is relatively small, which could potentially introduce biased sample selection and lead to certain

experimental conclusion errors, thus highlighting the inherent limitations. The authors look forward to conducting future multi-center, large-sample studies to further explore the impact of various risk factors on arterial stiffness, with the goal of enhancing the clinical application of pulse wave analysis.
The impetus for this study was derived from clinical issues, and the research findings hold relevance for the long-term medical management of common chronic diseases in a clinical setting.

5. Conclusion

By comparing the differences in carotid artery stiffness among the hypertension group, diabetes group, and normal control group, we found that hypertension is the chronic disease most likely to lead to carotid artery stiffness in comparison to diabetes.

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