

Study on the relationship between Cardio-cerebrovascular events and the level of Atherosclerosis evaluated by Heart-brain Integrated CTA

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Research

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Abstract

Background: To establish a one-stop cardio-cerebral vascular scanning technique based on double-source helical CT by analyzing the relationship between the nature of coronary artery, extracranial and extracranial vascular plaque, the degree of lumen stenosis and the occurrence and development of cardio-cerebrovascular disease (CCVD).

Methods: the plaque properties, vascular stenosis degree, and plaque quantitative analysis results of coronary artery, extracranial and intracranial segments of coronary artery, extracranial and intracranial carotid artery in 39 patients who underwent combined heart-brain CTA scanning were analyzed. The correlation between the load degree of cardio-cerebrovascular plaque and cardio-cerebrovascular events was analyzed comprehensively.

Results there were significant differences in age, high-density lipoprotein, diabetes, hypertension, smoking, plaque nature, plaque location, plaque composition and NIHSS score between the two groups.

Conclusion: the combination of heart and brain CTA can help to establish the best clinical predictive model to prevent and stop the occurrence and development of coronary heart disease and stroke in time.

1. Background

In recent years, stroke has become the number one killer threatening our national health. According to the results of a series of studies on the global burden of disease in 2018, despite the general increase in global life expectancy, the combined disease burden is getting heavier and heavier, and stroke has become the second leading cause of death in the world's population^{1, 2}. From a worldwide point of view, China is a high-risk area of stroke in the world. From a domestic point of view, stroke has replaced heart disease as the main cause of death and disability of adults in China. We believe that lumen stenosis, plaque shedding, and intra-plaque hemorrhage caused by carotid atherosclerosis are the main causes of stroke³. Some experiments have proved that there is a close relationship between carotid atherosclerosis and coronary artery atherosclerosis⁴. Nowadays, the concept of prevention has gradually taken root in the hearts of the people, and the main battlefield of cardio-cerebrovascular diseases has been gradually transformed into primary prevention⁵. The purpose of this study is to establish a one-stop cardio-cerebral macrovascular scanning process based on dual-source spiral CT and to establish a standard for evaluating plaque load. To establish a risk model of cardiovascular and cerebrovascular recurrence of extracranial and extracranial large artery stenosis based on whole-body plaque load measurement. Timely prevent and stop the occurrence and development of coronary heart disease and stroke.

2. Methods

2.1 Object

A total of 39 patients with suspected coronary heart disease or stroke who were admitted to our hospital in 2018.06 /2019.05 were examined by combined heart-brain CTA, and all patients were treated with standardized and optimized drug therapy. All patients were followed up at 3 and 6 months after onset, and the medication, vital signs, and cardiovascular and cerebrovascular events (ischemic stroke, coronary syndrome, vascular death) were recorded. All patients completed relevant laboratory tests within 24 hours of admission, such as blood glucose, HbA1C, D-dimer, four items of blood coagulation, LDL-C, HDL-C, TG, TCH, biochemical markers (CRP, hs-CRP, MMP2, MMP9, oxLDL-C, etc.). The inclusion criteria were: (1) age: 18 Mel 80 years old; (2) auxiliary examination (including carotid ultrasound TCD, head, and neck CTA or MRA) indicating intracranial artery stenosis; (3) patients with clinical symptoms suspected of coronary heart disease; (4) \geq two atherosclerotic risk factors (5) informed consent of patients and their families. The exclusion criteria were as follows: (1) patients with irregular heart rate could not complete combined heart and brain CTA examination (2) patients with PFO, atrial fibrillation, connective tissue disease, tumor and other non-atherosclerotic stroke, (3) head CT or MRI indicated hemorrhage, Large area cerebral infarction, or other diseases (vascular malformation, tumor, brain abscess, etc.); (4) patients with previous history of gastrointestinal ulcer who could not tolerate dual anti-platelet aggregation therapy with aspirin and clopidogrel, (5) patients with decreased liver and renal function (ALT, AST \geq 3 times normal high limit or creatinine F > 1.5mg/dl) or increased CK (\geq 10 times normal high limit); (6) allergic to aspirin, clopidogrel and statins, or could not be tolerated.

2.2 Inspection method

Siemens dual-source CT was used for large pitch scanning, the scanning range was from the other side to the top of the head, and the direction of the foot was scanned. FlashSpira mode is adopted. Pitch: 3.2, tube voltage 70mur90kV, tube current 330Mur450mAs, rotating speed 0.25s/ circle, collimation width: 0.6mm*96. Contrast agent iohexol 50ml was injected intravenously with 5ml/s, followed by saline 50ml at the same rate. The aortic root was selected to set the threshold for ROI, to 100HU, and the contrast tracer technique (Bolus-tracking method) was used to detect the density change of RIO. When the CT value of the RIO exceeded the threshold, the scan was triggered automatically with a delay of 8 seconds. The heart scan ECG triggers 30% or 65% of the cardiac cycle.

2.3 Image reconstruction and data post-processing

The collected data were processed by ADW4.6 workstation for various post-processing images, including volume rendering (VR), maximum density projection (MIP), curved surface reconstruction (CPR) reconstruction layer thickness of 0.75mm and spacing of 0.4mm. The best quality CTA images were analyzed for analysis and diagnosis. At the same time, the plaques of blood vessels were measured and quantitatively analyzed by the modified APQ (AUTOPLAQ) technique in all patients' images. The branch of the coronary artery is divided into three parts: the left trunk and left anterior descending branch, left circumflex branch, and the right coronary artery. The head and carotid artery is divided into four parts: the extracranial segment of the right head-carotid artery, the extracranial segment of the left head-carotid artery, the intracranial segment of the right head-carotid artery, and the extracranial segment of the left

head-carotid artery, including the aortic arch, the subclavian artery, the common carotid artery, the extracranial segment of the internal carotid artery and the extracranial segment of the vertebral artery. The intracranial segment of the cephalic carotid artery includes basilar artery, bilateral internal carotid artery, vertebral artery and anterior, middle and posterior cerebral arteries. For vessels with stenosis, the vessel diameter is measured by APQ vascular analysis software, and then according to the degree of stenosis, it can be divided into severe stenosis group (stenosis rate > 75%), moderate stenosis group (stenosis rate 50%-74%), mild stenosis group (stenosis rate < 50%). Vascular stenosis \geq 50% was defined as meaningful stenosis, and the degree of vascular stenosis was calculated. The degree of stenosis = (1 - the lumen area of the lesion site / the lumen area of the control site) x100%. It is found that the risk of plaque composition and its stability for atherosclerosis is much higher than that of arterial lumen stenosis¹⁴, so we further analyze the composition of plaque. Using the improved APQ non-calcified plaque detection technique, the plaque was divided into calcified plaque, non-calcified plaque and mixed plaque. We define non-calcified plaques and mixed plaques as unstable plaques. The indexes of non-calcified plaques were evaluated comprehensively.

2.4 Statistical analysis

SPSS statistical software was used to integrate and process the data. The measurement data were expressed as "x \pm s," the t-test of independent samples was adopted, and the counting data were analyzed by χ^2 , Cox regression method to analyze the correlation between various factors and cardio-cerebrovascular diseases.

3. Result

3.1 General information

Among the 39 patients in this study, there were 22 males (56%) and 17 females (44%). The age was 42- 83 years old, with an average of 65.6 \pm 12.5 years old. The clinical data of 39 patients with non-cardio-cerebrovascular diseases in the same period were selected as the control group, and all of them were examined by CTA. According to the occurrence of cardio-cerebrovascular events, patients were divided into two groups: patients with cardio-cerebrovascular events and those without cardio-cerebrovascular events.

3.2 CTA check result

There were 149 stable plaques and 124 unstable plaques in 39 patients by CTA. The CT value of calcified plaque was (523 \pm 242) HU, and that of the mixed plaque was (97 \pm 39) HU, The CT value of non-calcified plaque was (25 \pm 32) HU. CTA showed mild stenosis (145 cases), moderate stenosis (27 cases), severe stenosis (12 cases), and occlusion (3 cases).

Table 1 CTA shows Case group / control group plaque properties and stenosis statistics

	Plaque property	Normal	Degree of stenosis				Total
			Mild	Moderate	Severe	Block	
<i>Case group</i>	Stable plaque	52	83	13	1	0	149
	Unstable plaque	34	62	14	11	3	124
<i>control group</i>	Stable plaque	127	54	15	0	0	196
	Unstable plaque	30	32	12	3	0	77

3.3Cox regression analysis

Univariate analysis showed that there were significant differences in age, high-density lipoprotein, diabetes, hypertension, smoking, plaque nature, plaque location, plaque composition, and NIHSS score between cardio-cerebrovascular event group and non-cardio-cerebrovascular event group. (Table 2)

Table 2 Cox regression analysis of cardio-cerebrovascular events

	Univariate analysis		Multivariable analysis			
	Hazard ratio (95% CI)	p value	Model 1 ^a		Model 2 ^a	
			Hazard ratio (95% CI)	p value	Hazard ratio (95% CI)	p value
Demographics						
Age	0.86 (0.81-0.95)	<0.001	0.85 (0.82-0.95)	0.006	0.90(0.83-0.98)	0.012
Sex (men)	1.15(0.83-1.53)	0.443	1.33(0.98-1.81)	0.068	1.29(0.95-1.76)	0.100
Laboratory findings						
Hemoglobin, g/dL	1.04(1.02-1.06)	<0.001	1.02(1.01-1.03)	0.006	1.02(1.01-1.03)	0.007
Total cholesterol	0.82(0.72-0.97)	0.002	0.93(0.82-1.05)	0.368	0.93(0.81-1.07)	0.324
HDL cholesterol	0.74(0.45-1.20)	0.205				
LDL cholesterol	0.93(0.78-1.06)	0.186				
Medication at discharge						
Statin	0.54(0.21-1.42)	0.235				
Antihypertensive	0.73(0.44-1.16)	0.164				
Anticoagulant	1.13(0.83-1.49)	0.456				
Risk factors						
Hypertension	0.73(0.43-1.17)	0.164				
Diabetes mellitus	1.10(0.81-1.54)	0.451				
Atherosclerosis	1.05(0.97-1.09)	0.145				
INIHSS score	2.33(1.75-3.19)	<0.001	1.92(1.47-2.63)	<0.001	1.80(1.33-2.49)	<0.001
Current smoker	1.02(1.00-1.09)	<0.001	1.03(1.00-1.06)	0.002	1.06(1.02-1.09)	0.002
Extent of stenosis						
No stenosis	1		1			
Mild stenosis	1.36(0.98-2.05)	0.084	1.24(0.84-1.88)	0.201		
Moderate stenosis	1.43(0.94-2.29)	0.073	1.35(0.96-2.19)	0.142		
Severe stenosis	2.56(1.62-4.00)	<0.001	2.25(1.35-3.52)	0.001		
Block	4.10(2.60-6.47)	<0.001	2.92(1.80-4.60)	<0.001		
Plaque property						
Stable plaque	1.35(0.93-1.95)	0.087			1.25(0.87-1.83)	0.215
Unstable plaque	2.21(1.59-3.10)	<0.001			2.93(1.82-4.60)	<0.001

Model 1^a included the presence of CCVD as entering variables, whereas Model 2^a used the extent of CCVD.

3.4 quantitative analysis of plaques

All patients' images were measured and quantitatively analyzed by the modified APQ (AUTOPLAQ) technique (figure 1). The results of plaque quantitative analysis (Table 3) were compared in patients with the symptomatic cardio-cerebrovascular disease ((CCVD)). Based on the evaluation of systemic atherosclerosis, the risk

stratification index of cardiovascular events in symptomatic CCVD patients was established.

Table 3 quantitative analysis of plaques

Patch feature	No cardio-cerebrovascular events occurred	The occurrence of cardio-cerebrovascular events	P-value
NCP Volume	41.23±25.34	262.5±100.43	0.038
CP Volume	8.54±3.44	11.4±4.75	0.288
LD NCP Volume	35.65±17.48	66.3±24.53	0.011
Total Plaque Volume	66.3±12.76	273.9±43.87	<0.001
NCP Burden[%]	23.6±14.32	47.6±12.45	0.001
LD NCP Burden[%]	7.32±3.45	12.0±6.23	0.021
CP Burden[%]	1.0±1.51	2.1±1.21	0.018
Total Plaque Burden[%]	46.92±29.50	61.7±15.6	0.001
Remodeling Index	1.09±0.32	3.33±0.55	0.014
Diameter Stenosis[%]	20.51±18.32	33.2±24.98	0.021
Area stenosis[%]	23.58±14.65	57.2±38.37	0.002
Plaque Length	2.25±1.83	4.56±4.19	0.004
Contrast density drop[%]	25.65±6.31	35.1±5.87	0.034

4. Discussion

The results show that NCP Volume, Total Plaque Burden (%), Remodeling Index) is the risk factor of cardio-cerebrovascular events, among which Total Plaque Burden has the greatest risk. The combination of the three can be widely used in clinical practice to predict cardio-cerebrovascular events.

The nature of atherosclerotic plaque and lumen stenosis are significantly related to the occurrence of cardio-cerebrovascular events⁶. Therefore, by detecting and judging the degree of atherosclerosis, especially the stability of plaque, and combining with clinical NIHSS score and cardio-cerebrovascular risk factors, it is of great significance for clinical guidelines to prevent the occurrence of cardio-cerebrovascular events.

The commonly used clinical calcification score CACS refers to Agatston score⁷⁻⁹, its disadvantage is due to the partial volume effect, the small calcification plaque score is easy to change during reexamination, the improved APQ technique avoids this change. Keelan¹⁰ et al. pointed out that calcification score can be used as an independent predictor of future coronary events, and is superior to the degree of stenosis and traditional risk factors. There is also a strong correlation between coronary arteries and head and neck vessels¹¹. Cardio-cerebral combined CT angiography is a one-stop cardio-cerebrovascular combined

scanning on the basis of CTA, which greatly improves the image resolution, greatly shortens the scanning time and reduces the radiation dose; it can be used to scan the cardio-cerebral vessels of patients to meet the clinical needs.

Some experiments have proved that carotid artery disease has a high predictive value for coronary artery disease¹². Considering the characteristics of ultrasonic detection of carotid artery, such as non-invasive, convenient, repeatable and relatively cheap, when planning to use heart-brain integrated CTA to evaluate coronary artery and carotid artery disease, it is reasonable to exclude traditional risk factors for ultrasonic detection of carotid artery in advance, and it is not recommended or recommended to apply heart-brain integrated CTA to the physical examination of people without indications. In patients with multiple hard plaques or mixed plaques in the carotid artery, the examination of integrated heart-brain CTA may be more targeted¹³.

In this study, the technical advantages of the second generation dual-source CT large-pitch Flash model were used to obtain the lumen stenosis data of coronary artery and head-carotid artery and the calcification integral values of different parts, and to explore the relationship between head-carotid arteriosclerosis and coronary atherosclerosis. Our study found that the more risk factors of cardiovascular and cerebrovascular diseases such as male, older, smoking, hypertension, diabetes, hyperlipidemia, the greater the probability of cardiovascular and cerebrovascular events, the more likely it is to induce cardio-cerebrovascular events. In CTA examination, the lower the CT value of plaque with more lipid content, the higher the risk of plaque damage and secondary lesions. In addition, the post-processing software of CTA can measure the thickness of soft plaque and reflect the risk of plaque, which is helpful to evaluate the risk of cardiovascular and cerebrovascular events. At the same time, the degree of calcification can reflect plaque stability to a certain extent, so we can simply evaluate the plaque composition and calcification in clinical diagnosis to guide clinicians to choose the best treatment plan.

There are still many shortcomings in this study, such as limited sample size, the low exposure level of cardio-cerebrovascular diseases, lack of long-term follow-up, and follow-up comparison of imaging and clinical data.

In summary, this study used integrated heart-brain CTA scan to establish a risk prediction model for patients with symptomatic intracranial and extracranial stenosis based on whole-body plaque load score, so as to realize individualized treatment of intracranial arterial stenosis, optimize the allocation of medical resources, optimize the process of stroke prevention and treatment, improve medical efficiency and reduce stroke incidence and recurrence rate, which is of great significance to the secondary prevention of stroke.

5. Conclusions

In the process of clinical diagnosis, a one-stop CTA can well reflect the degree of atherosclerosis. And one-stop CTA has the advantages of short scanning time, low radiation dose, and good safety, which makes it an inspection method with broad application prospects. The improved APQ technique can more accurately analyze the non-calcified components in the plaque so that the plaque parameters can be obtained more accurately, which is helpful to comprehensively evaluate the plaque load of the coronary artery and head-carotid artery.

Abbreviations

CCVD: cardio-cerebrovascular disease; NIHSS: National Institute of Health stroke scale.

Declarations

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Authors' contributions

Huan Yu designed the experimental procedures and submitted the plan of the study to the ethical committee, then supervised the research carried out. Yue Zhang, Dong Zhu designed and conducted analyses based upon data methods. Kuai Duan, Yi Hu, Chunhua Song contributed to "Background" and "Discussion" sections. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

The research plan has been submitted to the ethics committee of Liangxiang Hospital, Fangshan District, Beijing for approval. The Committee issued a positive decision No. 2018-02 on August 31, 2018. The ethics committee of medical college is part of a large medical university in Beijing. The written informed consent for participation was obtained from the caregivers and relatives of all participants.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests

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Figures

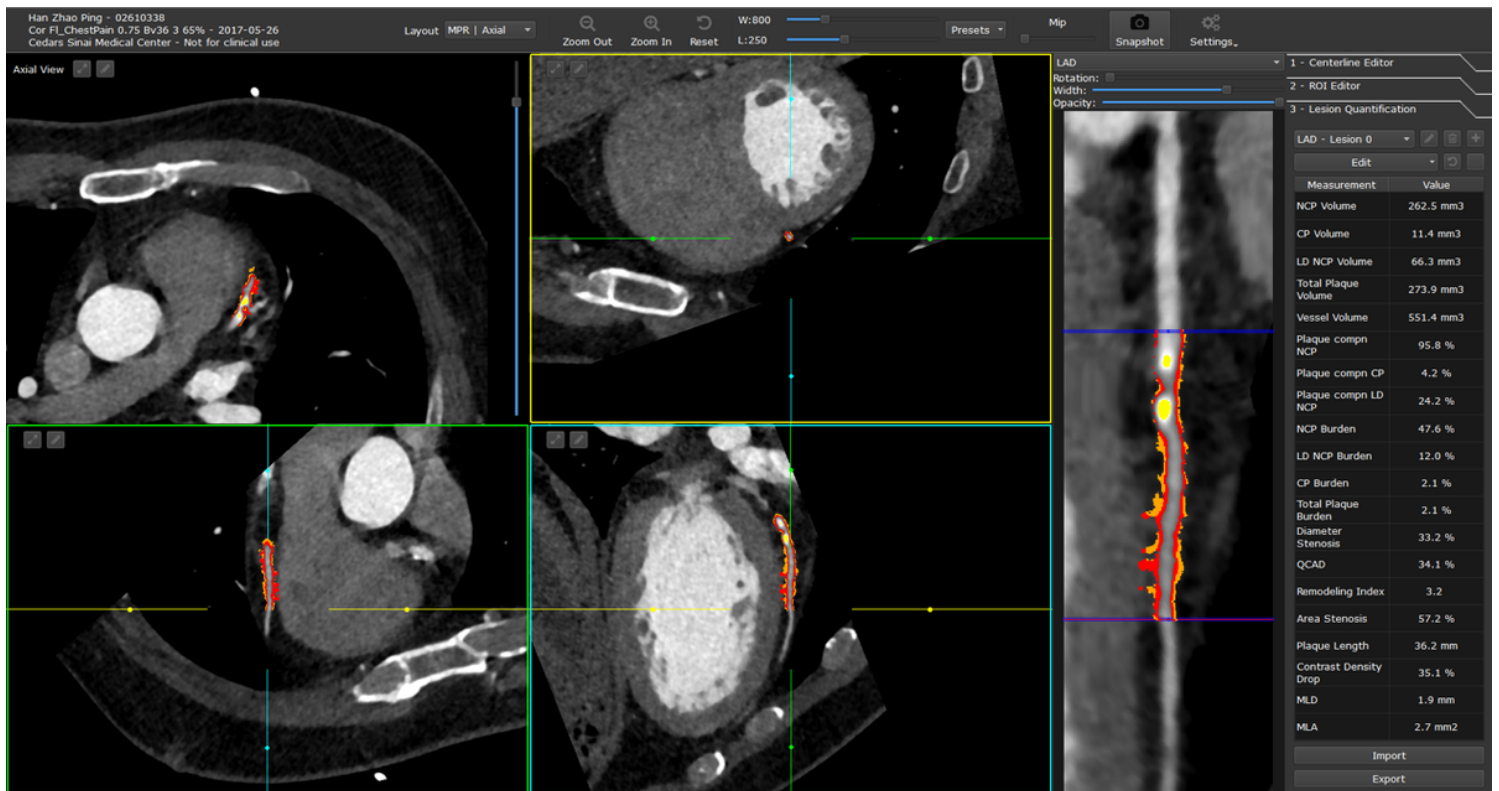


Figure 1

Measurement using improved APQ technique Lesion quantification: Red and orange for NCP, orange for Low-density NCP < 30 HU, Yellow for CP.