A Comparative Study of Clinical Characteristics Between Young and Elderly Patients with Coronary Slow Flow: Postprint

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Date: 2024-03-25T00:00:00+00:00

Abstract

Background The coronary slow flow (CSF) phenomenon manifests as recurrent resting angina, which may lead to severe cardiovascular events such as acute myocardial infarction, fatal arrhythmias, and sudden cardiac death, and impairs patients' quality of life. With the improved safety, feasibility, and reliability of coronary angiography (CAG), the detection rate of CSF has gradually increased; however, studies on the mechanisms of early-onset CSF and the clinical characteristics of young CSF patients are relatively scarce both domestically and internationally.

Objective To preliminarily investigate the clinical characteristics of young CSF patients and compare them with elderly CSF patients, thereby providing directions and insights for exploring the mechanisms of early-onset CSF.

Methods We consecutively analyzed 86 young patients (18 years $\leq$ age $<$ 45 years) hospitalized in the Department of Cardiology of the 305th Hospital of the Chinese People' s Liberation Army between January 2017 and January 2019 who were diagnosed with CSF via CAG as the young group, and randomly selected 88 CSF patients aged $\geq$ 65 years during the same period as the elderly group. Clinical data of patients in both groups, including medical history, diagnosis, and relevant laboratory examinations and CAG results, were collected and organized for comparative analysis.

Results The young group had lower mean age, proportions of hypertension and diabetes, and higher proportions of male patients and BMI than the elderly group ($P<0.05$). The number of CSF-affected vessels in the young group was predominantly single-vessel involvement (58.1%), whereas in the elderly group it was predominantly three-vessel involvement (45.5%); the difference in the distribution of the number of CSF-affected vessels between the two groups was sta-

tistically significant (2 =29.521, P<0.001). The total number of CSF-affected vessels was 137 in the young group and 199 in the elderly group; the difference in the distribution of CSF-affected vessels between the two groups was not statistically significant (2 =1.366, P=0.644). The levels of triglycerides (TG), serum uric acid (SUA), high-sensitivity C-reactive protein (hs-CRP), and endothelin-1 (ET-1) were higher in the young group than in the elderly group, while the level of nitric oxide (NO) was lower (P<0.05).

Conclusion Compared with elderly CSF patients, young CSF patients were more likely to be male and overweight, had fewer CSF-affected vessels, higher levels of TG, SUA, hs-CRP, and ET-1, and lower proportions of hypertension and diabetes. This suggests that metabolic abnormalities, inflammatory responses, and impaired vascular endothelial function are more closely associated with the pathogenesis of CSF in young patients.

Full Text

Comparative Study on Clinical Characteristics of Young and Elderly Patients with Slow Coronary Flow

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Abstract

Background: The coronary slow flow (CSF) phenomenon is characterized by recurrent angina pectoris at rest, which may lead to severe cardiovascular events such as acute myocardial infarction, fatal arrhythmias, and sudden cardiac death, while also reducing patients' quality of life. With improvements in the safety, feasibility, and reliability of coronary angiography (CAG), the detection rate of CSF has gradually increased. However, few studies have investigated the mechanisms of early-onset CSF and the clinical characteristics of young patients with this condition.

Objective: To explore the clinical characteristics of young patients with CSF and compare them with elderly patients, thereby providing direction for investigating the mechanisms of early-onset CSF.

Methods: We consecutively analyzed 86 young patients (18 ≤ age < 45 years)

diagnosed with CSF by CAG in the Department of Cardiology at the 305th Hospital of the People' s Liberation Army of China between January 2017 and January 2019, who were selected as the young group. During the same period, 88 CSF patients aged $\geq$ 65 years were randomly selected as the elderly group. Clinical data from both groups were collected and organized, including medical history, diagnosis, laboratory test results, and CAG findings, for comparative analysis.

Results: The young group had a lower mean age and lower proportions of hypertension and diabetes compared with the elderly group, while the male proportion and BMI were higher (P<0.05). The number of coronary vascular branches involved in CSF was predominantly single-vessel in the young group (58.1%), whereas three-vessel involvement was most common in the elderly group (45.5%). The distribution of affected vascular branches differed significantly between the two groups (^{2}=29.521, P<0.001). The total number of vessels affected by CSF was 137 in the young group and 199 in the elderly group, though the distribution of affected vessels showed no significant difference between groups (^{2}=1.366, P=0.644). The young group exhibited higher levels of triglycerides (TG), serum uric acid (SUA), high-sensitivity C-reactive protein (hs-CRP), and endothelin-1 (ET-1), and lower levels of nitric oxide (NO) compared with the elderly group (P<0.05).

Conclusion: Compared with elderly CSF patients, young CSF patients are more likely to be male and overweight, have fewer vessels involved, and show higher levels of TG, SUA, hs-CRP, and ET-1, but lower proportions of hypertension and diabetes. These findings suggest that metabolic abnormalities, inflammatory responses, and impaired vascular endothelial function are more closely associated with the pathogenesis of CSF in young adults.

Keywords: Coronary slow flow; Clinical characteristics; Young adult; Aged; Comparative study

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Introduction

The coronary slow flow (CSF) phenomenon refers to a condition where patients with recurrent chest pain show delayed distal coronary perfusion on coronary angiography (CAG) despite the absence of significant stenotic lesions in major coronary arteries (left anterior descending, left circumflex, and right coronary) [1-3]. CSF manifests as recurrent resting angina and may lead to serious cardiovascular events including acute myocardial infarction, fatal arrhythmias, and sudden cardiac death, while significantly reducing quality of life. As the safety, feasibility, and reliability of CAG have improved, the detection rate of CSF has gradually increased, with reported prevalence rates of 5.5%-34.0% among patients with suspected angina [4]. However, research on the mechanisms of early-onset CSF and the clinical characteristics of young patients remains limited both domestically and internationally. This study compares the clinical

characteristics of young and elderly CSF patients to provide insights into the mechanisms underlying early-onset CSF.

Methods

Study Population We consecutively enrolled 86 young patients (18 $\leq$ age $<$ 45 years) diagnosed with CSF by CAG in the Department of Cardiology at the 305th Hospital of the People' s Liberation Army of China between January 2017 and January 2019 as the young group (mean age 40.1 $\pm$ 5.9 years; 79 males, 7 females). During the same period, 88 CSF patients aged $\geq$ 65 years were randomly selected as the elderly group (mean age 68.7 $\pm$ 6.3 years; 62 males, 26 females). All participants provided informed consent.

Inclusion criteria: (1) Normal cognitive function; (2) Clinical symptoms of angina; (3) CAG confirming absence of significant coronary stenosis, with corrected TIMI frame count (CTFC) $\geq$ 27 frames in any one or more major coronary arteries (as determined by two experienced interventional cardiologists).

Exclusion criteria: (1) Myocardial bridging, myocardial infarction, history of coronary artery bypass grafting or percutaneous transluminal coronary angioplasty, or post-stent implantation; (2) Valvular heart disease, congenital heart disease, myocarditis, cardiomyopathy, or chronic pulmonary heart disease; (3) Coronary artery dissection, coronary spasm, or coronary aneurysmal dilation; (4) New York Heart Association (NYHA) functional class III or higher; (5) Hepatic or renal insufficiency; (6) Malignancy, autoimmune disease, or acute/chronic infection.

Data Collection General information and clinical data were collected. General information included age, sex, BMI, smoking history, and cardiovascular risk factors (hypertension, diabetes, hyperlipidemia). Clinical data comprised CAG results and laboratory test indicators.

Laboratory Tests After routine fasting for 12 hours, fasting venous blood samples were collected in the morning. Levels of fasting plasma glucose (FPG), total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), lipoprotein(a) [LP(a)], serum uric acid (SUA), high-sensitivity C-reactive protein (hs-CRP), endothelin-1 (ET-1), and nitric oxide (NO) were measured using an automatic biochemical analyzer (Beckman DXC800) and ELISA kits.

Statistical Analysis Data were analyzed using SPSS 22.0 software. Normally distributed continuous variables are expressed as mean $\pm$ standard deviation and compared between groups using independent samples t-tests. Non-normally distributed continuous variables are expressed as median (P25, P75) and compared using rank-sum tests. Categorical variables are expressed as frequencies and percentages, with between-group comparisons performed using ^{2} tests. Statistical significance was defined as $P<0.05$.

Results

Comparison of General Characteristics The young group had significantly lower mean age and lower proportions of hypertension and diabetes compared with the elderly group, while showing higher male proportion and BMI ($P<0.05$). No significant differences were observed between groups in smoking history or hyperlipidemia ($P>0.05$) .

Comparison of CAG Findings CSF involvement was predominantly single-vessel in the young group (58.1%), whereas three-vessel involvement was most common in the elderly group (45.5%). The distribution of affected vascular branches differed significantly between groups (^{2}=29.521, $P<0.001$) . The young group had 137 affected vessels total (left anterior descending: 62 [45.3%]; left circumflex: 33 [24.1%]; right coronary: 42 [30.6%]), while the elderly group had 199 affected vessels (left anterior descending: 88 [44.2%]; left circumflex: 51 [25.6%]; right coronary: 60 [30.2%]). The distribution of affected vessels did not differ significantly between groups (^{2}=1.366, $P=0.644$).

Comparison of Laboratory Indicators The young group exhibited significantly higher levels of TG, SUA, hs-CRP, and ET-1, and lower NO levels compared with the elderly group ($P<0.05$). No significant differences were found between groups in FPG, TC, HDL-C, LDL-C, or LP(a) levels ($P>0.05$) .

Discussion

CSF often represents an early manifestation of myocardial perfusion abnormalities or coronary atherosclerosis. Long-term follow-up studies indicate that CSF patients have an increased risk of developing coronary artery disease and acute myocardial infarction compared with angina patients with normal flow due to microvascular disease, with approximately one-third of CSF patients showing disease progression [5-8]. Our findings demonstrate that both the number and location of vessels affected by CSF were significantly higher in the elderly group than in the young group, highlighting the importance of preventing early-onset CSF and improving prognosis.

This study revealed that the young group had significantly higher proportions of male patients, overweight individuals, dyslipidemia, and elevated SUA levels compared with the elderly group. While many studies have attempted to evaluate the relationship between traditional cardiovascular risk factors and CSF, results have been inconsistent. Notably, the proportion of hypertension and diabetes was significantly lower in the young group, suggesting that other mechanisms contribute to CSF pathogenesis in young patients.

The young group showed markedly higher rates of overweight and dyslipidemia, with over 45.3% of patients having hyperlipidemia and significantly elevated serum TG levels. Current understanding suggests that elevated serum TG levels lead to smaller, denser HDL-C and LDL-C particles. Reduced HDL-C particle

size diminishes its protective effect against coronary disease, while small, dense LDL-C remnants and chylomicron remnants (TG-rich) more readily penetrate the arterial intima to form foam cells [9]. Zhao [10] emphasized that TG serves as a conditional risk factor for cardiovascular disease with significant value in risk assessment. The significantly higher TG levels in the young group suggest that hypertriglyceridemia promotes CSF development in young patients.

SUA levels were also significantly higher in the young group. Previous studies have identified elevated SUA as an independent risk factor for CSF formation, promoting coronary atherosclerosis progression [11-12]. As a purine metabolite, elevated SUA promotes release of oxygen free radicals, activates inflammatory cytokines, exacerbates vascular endothelial inflammatory stress, and allows SUA crystals to adhere to vascular walls, further damaging endothelial cells. These combined factors slow coronary blood flow and promote CSF progression.

Current research suggests that CSF pathogenesis involves microvascular disease, endothelial dysfunction, inflammatory responses, and abnormal platelet function and morphology. hs-CRP, an inflammatory biomarker synthesized by the liver, is elevated in CSF patients with myocardial damage and inflammatory infiltration [13-16]. The significantly higher hs-CRP levels in the young group indicate that inflammatory responses contribute to CSF development in young patients.

ET-1 is a vasoactive peptide synthesized and released by endothelial cells that serves as a vasoconstrictor and marker of vascular endothelial function [17]. NO is a key vasodilator produced in endothelial cells through oxidation of arginine via NO synthase activity, and reduced NO levels are associated with endothelial dysfunction [18-19]. The young group showed significantly higher plasma ET-1 levels and lower NO levels compared with the elderly group, suggesting that vascular endothelial dysfunction may be more prevalent in young patients and represents an important mechanism for early-onset CSF.

In summary, this study analyzed the clinical and CAG characteristics and laboratory biomarkers of young CSF patients (<45 years) and compared them with elderly patients. We found that young CSF patients were predominantly male, more likely to have single-vessel involvement, and showed higher rates of overweight, elevated SUA, dyslipidemia, vascular endothelial dysfunction, and inflammatory responses. These findings highlight the close relationship between these factors and CSF onset in young adults. Strengthening education and controlling risk factors in young people may help prevent early-onset CSF and improve prognosis. This study has limitations as a single-center study with a relatively small sample size, which may limit representativeness and introduce bias. Future multi-center, large-sample studies are needed to enhance the reliability of these findings.

Author Contributions

Wei Wei: Conceived the main research objectives, designed the study, and wrote the manuscript. Li Wei: Revised the manuscript. Li Wei and Du Dayong: Analyzed and interpreted coronary blood flow velocity for all enrolled patients. Jia Ning, Tong Haifeng, and Shi Liwei: Collected and organized data, performed statistical analysis, and prepared tables. Liu Chang: Responsible for quality control, overall article supervision, and management.

Conflict of Interest Statement: The authors declare no conflicts of interest.

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Received: December 10, 2023; Revised: March 11, 2024
Edited by: Kang Yanhui

Note: Figure translations are in progress. See original paper for figures.