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Cardiovascular Reviews

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Research Progress on Coronary Microvascular Diseases

Jieying Zhu*

Handan First Hospital, Handan 056002, China

***Corresponding author:** Jieying Zhu, sutra_2008@163.com

Abstract: Coronary microvascular disease (CMVD) is a multifactorial myocardial ischemia-angina condition mainly stemming from abnormalities in the structure and function of coronary microvessels. Currently, there is no specialized treatment for CMVD. Therefore, enhancing research on CMVD can generate insights for subsequent clinical development of personalized treatments. This article delves into the research progress of CMVD and comprehensively reviews its definition, classification, epidemiology, pathological mechanisms, non-drug treatments, and advancements in Western medicine and traditional Chinese medicine approaches.

Keywords: Coronary microvascular-related diseases; Pathological mechanism; Research progress

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1. Introduction

The coronary microcirculation encompasses arterioles, venules, and capillaries, constituting a microvascular system. Coronary microvascular disease (CMVD) predominantly involves extravascular mechanisms, with exertional angina serving as the primary indicator, often indicative of myocardial ischemia [1]. Principal manifestations of abnormal microcirculatory structure include reductions in vascular lumen diameter and microvessel density, leading to heightened microvascular resistance. Microcirculatory dysfunction manifests primarily through endothelial cell dependence, microvascular constriction, or embolism, alongside observable abnormalities in vasodilation [2]. External compression and tissue edema represent prevalent signs of extravascular changes, sometimes accompanied by a reduction in cardiac diastolic time. This article presents a review of recent advancements in CMVD treatment research.

2. Definition and classification of CMVD

The etiology of CMVD is multifaceted, encompassing various clinical syndromes characterized by objective evidence of abnormal structure and/or function of coronary arterioles and arterioles. Predominant clinical features include exertional angina or myocardial ischemia, often predisposing individuals to coronary artery

disease. Decreases in coronary flow reserve (CFR) are common, with myocardial ischemia symptoms frequently accompanying angina attacks. CMVD can be classified based on causative factors into three types: (1) CMVD without obstructive coronary artery disease, (2) CMVD combined with obstructive coronary artery disease, and (3) other CMVD subtypes. CMVD without obstructive coronary artery disease encompasses microvascular angina and slow coronary flow, while CMVD combined with obstructive coronary artery disease primarily presents as stable angina due to coronary heart disease, with instances of vascular recanalization but persistent myocardial perfusion without reflows following emergency percutaneous coronary intervention (PCI). Other CMVD subtypes include mechanisms associated with stress-induced, hypertrophic, dilated cardiomyopathy, aortic stenosis, and other conditions.

3. Epidemiology of CMVD

CMVD patients exhibit a heightened risk of major adverse cardiovascular events (MACE) compared to healthy individuals. CMVD also serves as an independent risk factor for diastolic dysfunction, often necessitating hospitalization due to complications with heart failure with preserved ejection fraction. Hence, prompt and effective diagnosis and treatment of CMVD are imperative. Despite limited large-scale randomized controlled trials focusing on CMVD treatment, future studies should expand sample sizes to furnish high-quality evidence.

4. Pathological mechanisms of CMVD

4.1. Abnormal coronary microvascular structure

Abnormalities in the coronary microvascular structure entail pathological changes within the microvessels of the coronary artery system. These abnormalities may disrupt microcirculation, consequently affecting myocardial perfusion and cardiac function. Increased left ventricular mass can precipitate changes in vascular structure, leading to microvascular remodeling. In conditions like hypertrophic cardiomyopathy, smooth muscle cell hypertrophy and collagen deposition can cause intimal and medial hypertrophy in interval arterioles, thereby reducing the lumen area. Atherosclerosis can further exacerbate microvascular obstruction and lumen narrowing [3], resulting in structural abnormalities such as stenosis, blockage, or fibrosis within coronary microvessels. These aberrations impede myocardial perfusion and nutrient supply, potentially precipitating cardiac symptoms like chest pain, shortness of breath, palpitations, and in severe cases, cardiovascular events such as myocardial infarction.

4.2. Abnormal coronary microvascular function

Coronary microvascular dysfunction can arise from multiple factors, including endothelial dysfunction, inflammation, excessive contraction, and ischemia-reperfusion injury. It typically manifests as normal coronary arteries with impaired microvascular function, leading to myocardial ischemia and other cardiac complications. Patients may experience symptoms such as angina pectoris, chest pain, shortness of breath, and fatigue, often accompanied by endothelial or smooth muscle dysfunction, microvascular spasm, obstruction, and heightened inflammatory response.

(1) Coronary endothelial dysfunction: This constitutes a pivotal factor in CMVD, wherein coronary endothelial cells, situated within coronary blood vessel walls, play a crucial role in vessel wall stability and function. Under normal conditions, endothelial cells regulate vessel relaxation and contraction by secreting bioactive substances, thereby maintaining vessel patency. Through the action of nitric oxide (NO), vascular endothelial cells can actively regulate vascular smooth muscle function, relax

large epicardial blood vessels and small blood vessels in the microcirculation, and promote increased coronary blood flow. However, in the presence of risk factors and atherosclerosis, endothelial cell damage and accelerated apoptosis occur, leading to endothelial dysfunction and impaired vasodilation response, subsequently affecting coronary blood flow.

(2) Vasoactive substances: Stimulating smooth muscle in CMVD patients can disrupt cell membrane receptors and intracellular signaling pathways, contributing significantly to smooth muscle diastolic dysfunction.

(3) Microvascular spasms: These spasms, often induced by sympathetic nerve dysfunction, can lead to a significant contraction of coronary microvessels, resulting in decreased myocardial perfusion and subsequently myocardial ischemia.

(4) Inflammation and microvascular embolism: Inflammation serves as a crucial clinical indicator for CMVD prediction, with systemic inflammatory response potentially inducing CMVD [4].

5. Diagnostic technology of CMVD

5.1. Non-invasive techniques

Non-invasive technologies, such as transthoracic Doppler echocardiography (TTDE), myocardial contrast echocardiography (MCE), cardiovascular magnetic resonance (CMR), and positron emission tomography (PET), estimate CFR and evaluate microvascular function. PET testing serves as the gold standard with CFR < 2. CMR serves as the primary tool for assessing the myocardial perfusion reserve index (MPRI). Additionally, CMR technology can assess myocardial blood flow (MBF) under varying resting and hyperemic states, offering an alternative method for evaluating coronary microvascular function.

5.2. Invasive technologies

Coronary angiography provides insight into microvascular function, although the examination period may be affected by coronary perfusion pressure and heart rate. The thermodilution method evaluates coronary microvascular function but may yield biased results due to differences in saline injection dose and speed, as well as uneven mixing with blood. Intracoronary Doppler guidewires measure blood flow velocity and CFR within coronary arteries, but the guidewire's position may affect blood flow velocity.

6. Non-drug treatment

6.1. Lifestyle intervention

A heart-healthy diet, low in saturated fat and cholesterol but rich in fruits, vegetables, whole grains, and healthy fats (such as olive oil and nuts), is recommended. Maintaining a healthy weight reduces cardiac burden and improves microvascular function. Moderate aerobic exercise (e.g., walking, cycling, swimming) enhances heart blood supply, cardiovascular health, and microvascular function. Timely detection and management of chronic conditions like hypertension and hyperglycemia can curb microvascular disease progression. Effective stress management is crucial for cardiovascular health, as prolonged emotional stress may impair microvascular function.

6.2. Mechanical methods during percutaneous coronary intervention

Utilizing balloons, filters, and thrombus aspiration devices during interventional procedures can prevent distal embolism post-percutaneous coronary intervention (PCI), enhancing myocardial microcirculation, promoting

reperfusion, and mitigating myocardial infarction risk.

6.3. Ischemic adaptation

Repetitive cuff inflation and deflation on the upper arm induce local ischemia, prompting vasodilator-active factor release to safeguard the myocardium. Repeated balloon use pre- and post-PCI may induce significant changes in myocardial perfusion and infarction size, highlighting its potential in managing coronary artery obstruction and myocardial ischemia.

7. Western medicine treatment

7.1. Improving microvascular structure

PCI exhibits a positive impact on angina pectoris in CMVD patients with obstructive coronary artery disease, fostering favorable recovery in coronary microcirculation. Sodium nitroprusside, a commonly utilized drug for no-reflow treatment, dilates arterioles, enhancing coronary microcirculation blood flow. Anisodamine, a tropane alkaloid extracted from some plants of the family *Solanaceae*, mitigates microvascular spasms, regulates coronary microcirculation, prevents ischemia/reperfusion injury, reverses coronary no-reflow, and promotes positive myocardial blood flow [5]. Effective coronary microvessel expansion can be achieved during PCI. Injecting sodium nitroprusside and anisodamine into coronary arteries enhances myocardial microcirculation. Standardized nitrate drug use yields significant outcomes in subepicardial coronary artery stenosis and spasm-related conditions. Rho kinase inhibitor Fasudil reduces microvascular spasms and angina attack frequency, while Nicorandil dilates subepicardial coronary arteries, alleviating symptoms in coronary microvascular angina patients and improving electrocardiogram exercise test results. Ivabradine and Ranolazine also ameliorate angina pectoris symptoms. Reducing atherosclerosis risk factors can enhance treatment efficacy in patients with stable angina pectoris. Effective hypoglycemia restores coronary microvascular endothelial function. Angiotensin-converting enzyme inhibitors (ACEI) and angiotensin receptor blockers (ARB) alter endothelial function and decrease myocardial oxygen demand, prolonging diastolic perfusion in hypertension patients.

7.2. Anti-myocardial ischemia/angina pectoris

β-blockers significantly reduce myocardial oxygen consumption, slowing ventricular rate, prolonging ventricular diastole, increasing ventricular diastolic volume, and enhancing coronary perfusion when standardized. They also exhibit antioxidant properties. Combining β-blockers with non-dihydropyridine calcium antagonists synergistically improves efficacy. Nitrate drugs effectively treat subepicardial coronary artery stenosis, but their efficacy in CMVD treatment is limited due to their inability to interact with nitrate-converting enzymes and NO receptors. Calcium ion antagonist drugs, particularly non-dihydropyridine types, slow heart rhythms and alleviate myocardial ischemia symptoms. Dihydropyridine types relax blood vessels and myocardium, increasing blood oxygen demand and relieving chest pain. ATP-sensitive potassium channel opener Nicorandil dilates coronary microvessels, improving electrocardiogram exercise test results, especially suitable for treating coronary microvascular angina. Other drugs like late sodium channel blockers (e.g., ranolazine) improve angina symptoms, left ventricular diastolic function, and CFR. Sinoatrial node pacing current blocker Ivabradine serves as an alternative therapy for β-blocker-intolerant individuals. Rho kinase inhibitor Fasudil, when used properly, inhibits microvascular spasms, reduces angina frequency, and holds significant pharmaceutical value [6].

8. Traditional Chinese medicine treatment

8.1. Traditional Chinese medicine decoction

Research by Wang *et al*. has demonstrated that the Liqi Huatan Huoxue prescription can effectively protect vascular endothelium and alleviate clinical symptoms by increasing serum NO concentration [7]. Li and colleagues studied CMVD patients with qi stagnation and blood stasis, selecting Huoxue Tongmai Yixin Decoction to swiftly enhance cardiac microcirculation and restore vascular endothelial function, thereby reducing angina symptoms [8]. Zheng and the team advocate for nourishing the Qi meridians and unblocking the heart meridians to address microcirculatory disorders, improving cardiac blood supply, and alleviating CMVD symptoms [9].

8.2. Chinese patent medicines

Treatment with Xinkeshu Tablets, as studied by Chen *et al*. [10], increases NO expression and decreases endothelin-1 levels in patient serum, significantly improving treatment outcomes for coronary microcirculation disorders. Peng and colleagues found that the Huayu Fuyuan Capsule reduced inflammatory responses, and enhanced coronary microcirculation endothelial function and activity tolerance, thereby improving CMVD patients' quality of life [11].

8.3. Other TCM method of treatment

Acupuncture, as demonstrated by Zhang *et al*. [12], effectively treats angina pectoris with minimal adverse effects. Acupoint application of traditional Chinese medicine formulas positively influences angina pectoris prevention and treatment, regulating lipids, improving endothelial function, and demonstrating significant anti-inflammatory effects. Traditional Chinese medicine aerosol treatment for CMVD offers rapid onset, portability, and high safety. Studies indicate that wide-chest aerosol improves angina symptoms, enhances electrocardiogram efficacy, and is well-tolerated and safe for patients [13].

9. Conclusion

CMVD serves as a risk factor for coronary heart disease and cardiovascular events. Tailoring personalized treatment plans based on patient conditions is crucial. Traditional Chinese medicine holds potential advantages in CMVD prevention and treatment, although the complexity of traditional Chinese medicine ingredients necessitates further high-quality clinical observations in subsequent studies.

Disclosure statement

The author declares no conflict of interest.

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The Effect of Percutaneous Coronary Intervention in Elderly Patients with Coronary Heart Disease and Its Impact on Cardiac Function Indicators

Wenlin Lu*

Department of Cardiovascular Medicine, Wuxi No.2 People's Hospital, Wuxi 214000, China

***Corresponding author:** Wenlin Lu, kinglwl@126.com

Abstract: *Objective:* To analyze the role of percutaneous coronary intervention and its value in elderly patients with coronary heart disease. *Methods:* A total of 88 elderly patients diagnosed with coronary heart disease between June 2022 and June 2023 were recruited and divided into two groups using the random number table method, with 44 cases in each group. The control group received conventional drug therapy, while the observation group received percutaneous arterial interventional treatment in addition to conventional drug therapy. Clinical efficacy, adverse cardiovascular events, cardiac function indicators, and quality of life were observed in both groups. *Results:* The observation group demonstrated a significantly higher total effective rate and significantly lower adverse cardiovascular events ($P < 0.05$). Furthermore, after treatment, the observation group showed a higher left ventricular ejection fraction, as well as lower left ventricular end-systolic diameter, left ventricular end-systolic volume, left ventricular end-diastolic diameter, and left ventricular end-diastolic volume ($P < 0.05$). Additionally, the observation group had higher scores in all eight dimensions of the SF-36 scale ($P < 0.05$). *Conclusion:* For elderly patients diagnosed with coronary heart disease, percutaneous coronary intervention can achieve superior clinical efficacy and high safety and can help improve cardiac function indicators and quality of life.

Keywords: Advanced age; Coronary heart disease; Percutaneous coronary intervention; Cardiac function indicators

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1. Introduction

Coronary heart disease is a cardiovascular disease resulting from the narrowing or blockage of blood vessels due to atherosclerotic lesions in the coronary arteries. The elderly constitute the primary demographic affected by this disease, with common contributing factors including dietary habits and high blood lipid levels [1]. Chest pain, often accompanied by dyspnea, represents the predominant symptom among patients with coronary heart disease, significantly impacting their quality of life [2]. Percutaneous coronary intervention stands as a standard

procedure aimed at ameliorating the condition of individuals with coronary heart disease. This interventional utilizes transradial catheter technology to alleviate stenosis or occlusion in coronary arteries, thereby facilitating the improvement of ischemic and hypoxic myocardial tissue [3]. In this study, percutaneous coronary intervention was carried out to evaluate its role and value in elderly patients with coronary heart disease.

2. Materials and methods

2.1. General information

A total of 88 elderly patients confirmed to have coronary heart disease following examination between June 2022 and June 2023 were recruited and divided into two groups using the random number table method, with 44 patients in each group. A comparison of clinical data among all patients revealed no significant difference ($P > 0.05$). The control group comprised 24 males and 20 females, aged 76 to 83 years old, with an average age of 79.40 ± 1.16 years. Cardiac function classification in this group included 15 cases of grade II, 14 cases of grade III, and 15 cases of grade IV. The observation group consisted of 25 males and 19 females, with ages ranging from 76 to 83 years old and a mean age of 79.24 ± 1.26 years. Cardiac function classification in this group included 13 cases of grade II, 15 cases of grade III, and 16 cases of grade IV.

Inclusion criteria: (1) Patients diagnosed with coronary heart disease via cardiac ultrasound and conventional surface electrocardiogram, aged over 75 years; (2) Patients' family members are informed of the study and voluntarily consent to participation.

Exclusion criteria: (1) Individuals with fatal arrhythmias; (2) Individuals with severe liver and kidney dysfunction; (3) Individuals with allergic reactions to the drugs used in this study; (4) Individuals with aortic dissection or cerebral hemorrhage; (5) Individuals with immune diseases and myocardial infarction; (6) Individuals with malignant tumors; (7) Individuals with contraindications to percutaneous coronary intervention.

2.2. Methods

The control group received conventional drug treatment, consisting of 100 mg aspirin (National Drug Approval No. J20130078, Bayer Healthcare Co., Ltd.) once daily and 75 mg clopidogrel [Sanofi (Hangzhou) Pharmaceutical Co., Ltd., national drug approval number J20130083] once daily or 90 mg ticagrelor (AstraZeneca) twice daily, continued for 30 days.

The observation group received percutaneous coronary intervention treatment in addition to conventional drug treatment 3 days before surgery. The percutaneous coronary intervention was performed on the radial artery. Patients were in the supine position, with the right upper limb extended outward 30°, the proximal and superior end of the radial styloid process was selected, and the pulsating radial artery was chosen as the puncture site. Local anesthesia was administered, followed by the insertion of a 5F arterial sheath for coronary angiography. 100 U/kg heparin sodium [Sanofi (Beijing) Pharmaceutical Co., Ltd.] was administered. The sheath was removed, and hemostasis was performed using a radial artery compressor. Post-surgery, 5,000 U of low-molecular-weight heparin sodium was subcutaneously injected daily for seven days.

2.3. Observation indicators

(1) Clinical efficacy: The number of angina attacks is reduced by more than 90% after treatment, nitroglycerin is no longer needed, and the tolerance of daily activities significantly increased are considered "markedly effective"; The number of angina attacks is reduced by 50% after treatment, the dosage of nitroglycerin can be reduced by more than 50% for 90% of the angina attacks, and increasing

daily activity tolerance are considered "effective"; The first two standards not met are considered "ineffective". Total efficacy is the sum of markedly effective and effective cases.

(2) Adverse cardiovascular events: Arrhythmia, myocardial infarction, and deterioration of cardiac function of both groups were recorded.

(3) Cardiac function indicators: Cardiac function is detected through cardiac color Doppler ultrasound examination, including the following indicators: left ventricular ejection fraction (LVEF), left ventricular end-systolic diameter (LVESD), left ventricular end-systolic volume (LVESV), left ventricular end-diastolic diameter (LVEDD), and left ventricular end-diastolic volume (LVEDV).

(4) Quality of life scores: Patient quality of life is evaluated using the SF-36 score, which contains 8 scales: physiological function (PF), bodily pain (BP), role limitations due to physical health problems (RP), role limitations due to personal or emotional problems (RE), general mental health (MH), social functioning (SF), energy/fatigue or vitality (VIT), and general health perceptions (GH). The total score of each dimension is 100 points. A higher SF-36 score indicated a better quality of life.

2.4. Statistical analysis

Statistical analysis was performed using SPSS 28.0 software. Measurement data were expressed as mean ± standard deviation (SD) and compared using the *t*-test, whereas count data were presented as [*n* (%)] and compared using the χ^2 test. A statistically significant difference was defined as $P < 0.05$.

3. Results

3.1. Clinical efficacy and adverse cardiovascular events

Table 1 shows that the observation group had a significantly higher total effective rate and significantly lower adverse cardiovascular event rate ($P < 0.05$).

Table 1. Analysis of the total effective rate and incidence of adverse cardiovascular events in the two groups [*n* (%)]

		Control group (*n* = 44)	Observation group (*n* = 44)	χ^2	P
Clinical efficacy	Markedly effective	17 (38.64)	25 (56.82)		
	Effective	13 (29.55)	19 (43.18)		
	Ineffective	14 (31.82)	3 (6.82)		
	Total efficacy	30 (68.18)	41 (93.18)	8.822	0.003
Adverse cardiovascular events	Arrhythmia	4 (9.09)	1 (2.27)		
	Myocardial infarction	4 (9.09)	1 (2.27)		
	Deterioration of heart function	4 (9.09)	2 (4.55)		
	Total incidence rate	12 (27.27)	4 (9.09)	4.889	0.027

3.2. Cardiac function indicators

As shown in **Table 2**, there were no significant differences in cardiac function indicators between both groups before intervention ($P > 0.05$). However, after intervention, the observation group exhibited a significantly higher LVEF, and significantly lower LVESD, LVESV, LVEDD, and LVEDV, as compared to the control group ($P < 0.05$).

Table 2. Analysis of cardiac function indicators in the two groups (mean ± SD)

Cardiac function indicators	Before intervention (n = 60)		t	P	After intervention (n = 60)		t	P
	Control group	Observation group			Control group	Observation group		
LVEF (%)	40.54 ± 5.39	41.37 ± 5.19	0.447	0.118	45.25 ± 4.62	55.41 ± 5.39	13.167	0.001
LVESD (mm)	42.35 ± 4.50	42.45 ± 4.32	0.649	0.402	38.62 ± 6.23	30.14 ± 5.47	12.127	0.001
LVESV (mL)	61.54 ± 7.35	60.15 ± 8.22	0.910	0.343	55.67 ± 8.15	48.32 ± 6.40	8.961	0.001
LVEDD (mm)	61.37 ± 8.06	61.70 ± 8.26	0.099	0.782	54.19 ± 5.75	44.35 ± 5.15	11.049	0.001
LVEDV (mL)	163.44 ± 17.50	164.30 ± 17.52	0.018	0.763	101.64 ± 11.49	95.75 ± 10.31	9.392	0.001

3.3. Two groups of statistical analysis of life indicators

Both groups had similar quality of life scores during pre-treatment ($P > 0.05$). However, after treatment, the observation group had higher scores in 8 dimensions of SF-36 ($P < 0.05$), as presented in **Table 3**.

Table 3. Analysis of SF-36 scores of two groups (points, mean ± SD)

	Before intervention (n = 60)		t	P	After intervention (n = 60)		t	P
	Control group	Observation group			Control group	Observation group		
PF	56.24 ± 5.60	56.72 ± 5.39	0.265	0.647	66.42 ± 5.39	78.41 ± 5.20	7.943	0.001
BP	56.71 ± 5.30	56.45 ± 5.19	0.333	0.294	66.32 ± 5.10	75.49 ± 4.20	7.981	0.001
RP	56.80 ± 5.27	56.21 ± 5.58	0.216	0.725	65.92 ± 5.05	78.46 ± 4.29	8,686	0.001
GH	49.72 ± 5.60	49.60 ± 5.34	0.441	0.363	67.32 ± 5.11	79.14 ± 4.25	8,086	0.001
VIT	51.24 ± 5.26	51.46 ± 5.19	0.225	0.353	62.67 ± 5.09	77.13 ± 4.08	8.410	0.001
SF	50.39 ± 5.45	50.37 ± 5.29	0.176	0.853	65.37 ± 5.10	78.41 ± 4.32	9.390	0.001
RE	50.19 ± 5.27	50.26 ± 5.40	0.098	0.892	65.39 ± 5.42	77.31 ± 4.15	9.990	0.001
MH	51.64 ± 5.47	51.37 ± 5.48	0.461	0.853	64.33 ± 5.19	77.41 ± 4.28	6.305	0.001

4. Discussion

The incidence of coronary heart disease has been on the rise in recent years, attributed to various factors. Common symptoms such as angina and palpitations are indicative of coronary heart disease, with severe cases posing a risk of fatality. Consequently, prompt intervention is crucial to treat elderly patients and halt disease progression [4].

Currently, both conservative drug therapy and surgical intervention are widely employed for coronary heart disease treatment. However, drug treatment's drawback lies in its slow onset of action [5]. In contrast, percutaneous coronary intervention offers a rapid and favorable outcome in clearing coronary lumens. This method utilizes transradial catheter technology to enhance myocardial blood perfusion, thereby alleviating myocardial ischemia and oxygen deficiency symptoms [6]. This study, focusing on clinical efficacy, cardiac function, and quality of life, indicates that percutaneous coronary intervention yields promising results. By relieving coronary artery stenosis or obstruction, this intervention facilitates coronary blood flow reconstruction and effectively alleviates clinical symptoms [7].

Moreover, percutaneous coronary intervention is minimally invasive, employing transradial catheter technology to deploy balloon catheters or other devices for expanding stenotic coronary arteries and implanting stents. This approach aids in ameliorating coronary artery stenosis and restoring normal coronary and

myocardial blood supply, thereby enhancing patient prognosis [8]. Previous research has demonstrated the benefits of percutaneous coronary intervention in improving cardiac function post-relief of myocardial ischemia and hypoxia [9]. Another study revealed that the insertion of a special balloon catheter into the coronary artery lesion dilates the stenotic blood vessel, thereby reconstructing the anatomical structure of the blood vessel, improving the necrotic myocardium, reducing the impact and symptoms of the condition, inhibiting disease progression to a certain extent, and reducing the risk of adverse cardiovascular events [10].

In summary, percutaneous coronary intervention emerges as an effective, safe, and life-saving intervention for elderly patients with coronary heart disease, significantly enhancing cardiac function indicators.

Disclosure statement

The author declares no conflict of interest.

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Sequential Treatment of Acute Heart Failure in the Elderly: Efficacy of Recombinant Human Brain Natriuretic Peptide and Sacubitril-Valsartan

Zhen Huang*

Jiangyin Fourth People's Hospital, Jiangyin 214421, China

***Corresponding author:** Zhen Huang, collin2_1985@163.com

Abstract: *Objective:* To explore the clinical efficacy of recombinant human brain natriuretic peptide (rhBNP) and sacubitril-valsartan in the sequential treatment of acute heart failure (AHF) in older individuals. *Methods:* Clinical data from 64 older patients with AHF were collected for this study. The patients were divided into two groups: a control group (Group A, $n = 34$) and an observation group (Group B, $n = 30$) based on different treatment regimens. Group A received rhBNP treatment, while Group B received sequential treatment with rhBNP and Sacubitril-Valsartan. The evaluation of the sequential treatment's effect on older patients with AHF was conducted using various indicators. *Results:* The clinical efficacy rate in Group A (93.33%) was significantly higher than that in Group A (73.53%), with a significant difference observed ($P < 0.05$). Furthermore, after treatment, the clinical efficacy remained significantly higher in Group B than in Group A. Group B exhibited a significantly higher left ventricular ejection fraction (LVEF) and significantly lower systolic blood pressure, diastolic blood pressure, and heart rate compared to Group A ($P < 0.05$). Although the left ventricular end-diastolic diameter (LVEDD) was lower in Group B after treatment, the difference was not statistically significant ($P = 0.127$). Moreover, post-treatment levels of NT-proBNP were significantly lower in Group B compared to Group A ($P = 0.01$). Additionally, Group B had shorter hospitalization times, faster improvement in clinical symptoms, and further 6-minute walking distances after the treatment compared to Group A ($P < 0.01$). *Conclusion:* Sequential treatment with rhBNP and Sacubitril-Valsartan demonstrates promising therapeutic effects in older patients with AHF, suggesting its potential for broader adoption and promotion in clinical practice.

Keywords: Recombinant human brain natriuretic peptide (rhBNP); Sacubitril-Valsartan; Sequential treatment; Elderly; Acute heart failure (AHF)

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1. Introduction

The aging process of society is accelerating, leading to acute heart failure (AHF) among the elderly, which poses a significant threat to their health and quality of life [1]. The treatment of AHF in older patients is complex and dynamic due to their physiological characteristics and the presence of multiple complications.

Therefore, the discovery of more effective and safer treatment methods is crucial for improving the therapeutic outcomes and quality of life of elderly AHF patients. Recombinant human brain natriuretic peptide (rhBNP), an endogenous cardiac hormone, has been shown in numerous studies to alleviate symptoms and enhance the quality of life in elderly AHF patients through various pathways, including its diuretic effects and its ability to reduce cardiac preload and afterload [2]. Sacubitril-Valsartan, a novel cardiovascular drug, has demonstrated efficacy in improving clinical symptoms and prognosis by inhibiting the effects of angiotensin receptors and neutral endopeptidase. Recently, the efficacy of sequential treatment with rhBNP and Sacubitril-Valsartan in older patients with AHF has garnered attention in clinical medical research. This treatment strategy aims to capitalize on the synergistic effects of both drugs and offer a more effective treatment option for elderly AHF patients by comprehensively regulating cardiovascular function. Building upon this premise, this article undertakes an in-depth examination of the efficacy of sequential treatment with rhBNP and Sacubitril-Valsartan in elderly AHF patients, intending to provide a more scientific basis and reference for the comprehensive treatment of this population.

2. Materials and methods

2.1. General information

Clinical data of 64 elderly AHF patients enrolled in the study were collected and categorized into a control group (Group A, n = 34) and an observation group (Group B, n = 30) based on distinct treatment protocols. Inclusion criteria comprised: (1) Patients aged 60 years or older; (2) Patients meeting relevant diagnostic criteria for AHF; (3) Patients with relatively stable conditions suitable for pharmacological intervention; (4) Patients without significant liver, kidney, or other organ dysfunction; (5) Patients with no history of allergy to rhBNP or Sacubitril-Valsartan; (6) Patients providing informed consent, understanding the research's purpose, methods, and risks, and willing to participate. Exclusion criteria included: (1) Patients under the age of 60; (2) Patients with an unclear diagnosis of AHF or other serious heart conditions (e.g., myocardial infarction, valvular heart disease); (3) Patients with severe liver and kidney dysfunction, incomplete disease profiles, malignant tumors, or other significant conditions potentially impacting study outcomes; (4) Patients with known allergies to any component of rhBNP or Sacubitril-Valsartan; (5) Patients with implanted permanent pacemakers; (6) Patients with a history of cardiac surgery; (7) Patients unable to complete the entire research process or with incomplete data records, thereby compromising analysis and evaluation of research results.

2.2. Methods

Upon admission, all patients received standard treatment. Group A received rhBNP treatment in addition to conventional treatment. RhBNP was administered intravenously within 24 hours of onset, followed by continuous intravenous infusion of 0.0075 μg/kg/min for 3–5 days. Group B received sequential treatment with rhBNP and Sacubitril-Valsartan alongside conventional therapy. Sacubitril-Valsartan was orally administered, initially at a dose of 50 mg twice a day, and increased to double dosage after 4 weeks and continued for 1 month.

2.3. Observation indicators

This study comprehensively assessed patients' clinical efficacy based on their symptoms and utilized systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR), left ventricular ejection fraction (LVEF), and left ventricular end-diastolic diameter (LVEDD) to evaluate blood pressure and cardiac function. N-terminal pro-brain natriuretic peptide (NT-proBNP) precursor was employed to assess AHF status, while hospitalization duration, time to clinical symptom improvement, and 6-minute walking distance post-treatment were used to

evaluate clinical efficacy.

2.4. Statistical analysis

Data processing was performed using SPSS 20.0, with measurement data expressed as mean ± standard deviation (SD) and count data expressed as [*n* (%)]. The independent sample *t*-test was utilized for normally distributed data, while the χ^2 test was employed for intergroup comparison of categorical data. A significance level of $P < 0.05$ indicated statistical significance.

3. Results

3.1. Clinical efficacy

Table 1 shows that the clinical efficacy rate of patients in Group B (93.33%) is significantly higher than Group A (73.53%; $P = 0.036$).

Table 1. Comparison of clinical efficacy [*n* (%)]

Indicator	Group A (*n* = 34)	Group B (*n* = 30)	χ^2	*P*
Markedly effective	9 (26.47%)	17 (56.66%)	-	-
Effective	16 (47.06%)	11 (36.67%)	-	-
Ineffective	9 (26.47%)	2 (6.67%)	-	-
Total effectiveness	25 (73.53%)	28 (93.33%)	4.392	0.036

3.2. Blood pressure and cardiac function indicators

As shown in **Table 2**, Group B shows a significantly higher LVEF, and significantly lower SBP, DBP, and HR after treatment as compared to Group A ($P < 0.05$). Group B's LVEDD appeared to be lower than Group A's but the difference is not statistically significant ($P = 0.127$).

Table 2. Comparison of blood pressure and cardiac function indicators (mean ± SD)

Indicator	Time	Group A (*n* = 34)	Group B (*n* = 30)	*t*	*P*
SBP (mmHg)	Before treatment	128 ± 9	130 ± 8	0.934	0.354
	After treatment	120 ± 7	112 ± 7	4.563	0.000
DBP (mmHg)	Before treatment	78 ± 7	79 ± 7	0.570	0.571
	After treatment	73 ± 6	70 ± 5	2.156	0.035
HR (beats/min)	Before treatment	118 ± 15	117 ± 16	0.258	0.797
	After treatment	86 ± 9	79 ± 6	3.609	0.001
LVEF (%)	Before treatment	39.64 ± 3.51	39.89 ± 3.64	0.280	0.781
	After treatment	48.25 ± 4.20	51.69 ± 5.01	2.988	0.004
LVEDD (mm)	Before treatment	50.63 ± 6.78	51.26 ± 6.77	0.371	0.712
	After treatment	47.69 ± 6.23	45.32 ± 5.99	1.546	0.127

3.3. Laboratory indicators

After treatment, the NT-proBNP level of Group B was significantly lower than Group A ($P < 0.01$), as presented in **Table 3**.

Table 3. Comparison of laboratory indicators (mean ± SD)

Indicator	Time	Group A (n = 34)	Group B (n = 30)	t	P
NT-proBNP	Before treatment	1,468 ± 165	1,481 ± 163	0.316	0.753
	After treatment	1,264 ± 143	1,101 ± 135	4.672	0.000

3.4. Clinical efficacy indicators

Group B showed shorter hospitalization duration and clinical symptom improvement time as compared to Group A ($P < 0.05$), and a further 6-minute walking distance post-treatment as compared to Group A ($P < 0.01$; **Table 4**).

Table 4. Comparison of clinical efficacy indicators (mean ± SD)

Indicator	Group A (n = 34)	Group B (n = 30)	t	P
Length of stay	13.29 ± 2.65	11.53 ± 2.01	2.962	0.004
Clinical symptom improvement time	5.68 ± 1.12	4.82 ± 0.72	3.599	0.001
Status of a 6-min walk after treatment	346.35 ± 32.15	368.65 ± 35.36	2.643	0.010

4. Discussion

AHF manifests as a rapid decline in cardiac function, resulting in diminished cardiac output, tissue and organ hypoperfusion, and acute congestion syndrome. It typically arises from abnormalities in cardiac structure or function, leading to myocardial contractility impairment and reduced cardiac output, ultimately culminating in pulmonary or systemic circulation congestion [3]. Various factors such as acute myocardial infarction, arrhythmia, heart valve disease, acute severe myocarditis, pericardial disease, hypertension, and diabetes can contribute to AHF [4]. Symptoms commonly include dyspnea (exertional dyspnea, orthopnea, paroxysmal nocturnal dyspnea), cough, sputum production, hemoptysis, fatigue, dizziness, palpitations [5], and in some cases, oliguria and renal impairment. Physical examination may reveal an elevated heart rate, galloping rhythm at the apex, lung crackles, jugular vein distension, hepatomegaly, and edema. This condition poses a significant threat to patients' lives, particularly among the elderly. Firstly, elderly individuals with AHF often present with multiple organ failure due to declining physical function, complicating treatment and exacerbating the disease. Secondly, dyspnea in elderly AHF patients may be more pronounced, severely impacting their quality of life. Dyspnea can hinder patients' ability to lie down or engage in daily activities, increasing the risk of falls and fractures. Additionally, AHF in the elderly may lead to cerebral ischemia, resulting in symptoms such as altered consciousness, syncope, and shock, potentially causing irreversible brain damage in severe cases. Furthermore, when treating AHF in the elderly, reduced liver and kidney function, among other factors, diminishes drug metabolism and excretion, heightening the risk of drug accumulation and adverse reactions, thereby complicating treatment.

Drug therapy constitutes the primary treatment modality for AHF patients. Diuretics are commonly employed to promote diuresis and alleviate lung and systemic congestion, while angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor blockers (ARBs) dilate blood vessels, lower blood pressure, and reduce cardiac workload. Beta-blockers are also utilized to decrease heart rate and myocardial oxygen consumption. In recent years, novel drugs such as rhBNP and Sacubitril-Valsartan have introduced new therapeutic strategies for AHF [6]. RhBNP, structurally and functionally akin to endogenous brain natriuretic

peptide, dilates blood vessels, lowers blood pressure, and reduces cardiac workload by binding to natriuretic peptide receptors, thereby improving clinical symptoms and prognosis in AHF patients. In older AHF patients, rhBNP rapidly alleviates cardiac workload, improves cardiac function, and reduces rehospitalization and mortality rates [7]. Sacubitril-Valsartan, an angiotensin receptor neprilysin inhibitor, inhibits angiotensin receptors and neprilysin activity, exerting antihypertensive, anti-cardiac hypertrophy, and anti-fibrotic effects. In older AHF patients, Sacubitril-Valsartan application enhances cardiac function and quality of life while decreasing rehospitalization and mortality rates.

Sequential therapy represents an optimized treatment model that sequentially administers different drugs to achieve enhanced therapeutic effects. Sequential treatment with rhBNP and Sacubitril-Valsartan maximizes therapeutic efficacy by harnessing the advantages of both drugs. In this study, patients in Group B, who received sequential treatment with rhBNP and Sacubitril-Valsartan, demonstrated significantly better clinical efficacy, blood pressure, cardiac function, and laboratory indicators compared to those in Group A, treated with rhBNP alone. Numerous studies corroborate these findings. Huang *et al*. reported that sequential treatment with rhBNP and Sacubitril-Valsartan yields superior clinical outcomes compared to rhBNP monotherapy for AHF [8]. Guo *et al*. similarly found that sequential treatment improves cardiac function and quality of life in AHF patients [9]. Additionally, Liu and colleagues suggested that sequential therapy reduces adverse reactions and enhances safety [10].

Nevertheless, this study has certain limitations. Firstly, the relatively small sample size may yield biased conclusions, warranting caution in interpreting the results. Secondly, AHF in the elderly is a chronic condition necessitating long-term observation and evaluation, yet this study only assessed treatment effects within one month, lacking long-term follow-up data. Future research should address these limitations by expanding sample sizes to enhance result stability and reliability. Additionally, studies should ensure sample diversity and representativeness to more accurately reflect real-world elderly AHF scenarios. Long-term follow-up observations are also imperative to assess sequential treatment's impact on patients' long-term prognosis, providing a more robust basis for clinical practice.

In conclusion, sequential treatment with rhBNP and Sacubitril-Valsartan achieves favorable therapeutic outcomes in older AHF patients, meriting broader adoption and promotion.

Disclosure statement

The authors declare no conflict of interest.

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A Case in Which Identification of Cardiac Scar Tissue by MDCT Was Effective in Ablation for Ventricular Tachycardia – A Secondary Publication

Takahiro Iseda[1], Kouji Hanazawa[1]*, Akihira Suenaga[1], Hiroyuki Kobayashi[2], Seiji Shima[3], Tomonari Kuribayashi[3], Mamoru Toyofuku[1]

[1]Department of Cardiology, Japanese Red Cross Wakayama Medical Center, Wakayama City 640-8558, Japan
[2]Department of Radiology, Japanese Red Cross Wakayama Medical Center, Wakayama City 640-8558, Japan
[3]Department of Laboratory, Japanese Red Cross Wakayama Medical Center, Wakayama City 640-8558, Japan

Corresponding author: Kouji Hanazawa, kouji8738@gmail.com

Abstract: During catheterization of ventricular tachycardia, it is often found difficult to identify the origin of ventricular tachycardia when tachycardia is not induced during the procedure or hemodynamics are disrupted. Late gadolinium enhancement (LGE) in cardiac MRI and late Iodine enhancement (LIE) in cardiac CT are reportedly performed to identify myocardial scar tissue and estimate the origin of ventricular tachycardia preoperatively. However, although LGE is useful for identifying the origin of tachycardia, the slice thickness is large and imaging takes a long time, and if a premature beat occurs or the device is inserted during imaging, a good image cannot be obtained. On the other hand, LIE also has poor resolution, making it difficult to take clear images. In this case report, the origin of ventricular tachycardia was presumed preoperatively using a new image processing method called Subtraction Myocardial Image for Late Iodine Enhancement (SMILIE) using a 320-row Area Detector CT, which was useful during catheter ablation.

Keywords: Multi Detector-row CT; Delayed enhancement imaging; Ventricular tachycardia

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1. Introduction

Ventricular tachycardia (VT) is widely recognized as a life-threatening arrhythmia and is often treated with catheter ablation in recent years. However, the success rate is only about 60% [1], which is not necessarily high. One reason for this is the difficulty in identifying the origin and circuit of VT. In catheter ablation therapy, VT is generally induced, and its origin and circuit are identified during VT for treatment. However, there are many problems such as the patient's hemodynamics deteriorating during the identification of the circuit of tachycardia or tachycardia itself not being induced at all.

Therefore, there have been reports [2-5] suggesting that myocardial scars depicted by late gadolinium enhancement (LGE) in cardiac MRI or late iodine enhancement (LIE) in cardiac CT are related to the origin of VT, and attempts have been made to identify the origin of VT using them. However, there are still many challenges such as the long duration of delayed enhancement MRI or CT imaging and the resulting unclear images.

At the Japanese Red Cross Wakayama Medical Center, cases have been experienced where catheter ablation therapy for ventricular tachycardia proved useful by clearly depicting myocardial scar tissue using a new CT image processing method called Subtraction Myocardial Image for Late Iodine Enhancement (SMILIE) [6]. As far as know, there have been no case reports of successful catheter ablation therapy for VT using SMILIE in the past, and this is the first report.

2. Case presentation

The patient is a 76-year-old male with a chief complaint of palpitations. He has no significant past medical history, medications, or family history. Additionally, he has no history of smoking and no known allergies.

Present illness: The patient has been experiencing palpitations for about a week. He noticed shortness of breath when climbing stairs a few days ago and presented at the Japanese Red Cross Wakayama Medical Center.

Physical examination on admission: Height 156.2 cm, weight 58.2 kg, blood pressure 156/98 mmHg, heart rate 205 beats/min, respiratory rate 30 breaths/min, temperature 37.3°C, percutaneous oxygen saturation 92% (room air), alert and oriented, no conjunctival pallor, no scleral icterus, no cardiac murmurs, clear lung sounds, flat abdomen, no tenderness or rebound tenderness, no bilateral lower leg edema.

Laboratory findings: AST 63 U/L, ALT 69 U/L, LDH 261 U/L, Alb 3.3 g/dL, BUN 30 mg/dL, Cre 1.72 mg/dL, CK 111 U/L, serum Na 136 mEq/L, serum K 4.2 mEq/L, serum Cl 107 mEq/L, blood glucose 145 mg/dL, HbA1c 5.5%, WBC 10800/μL, RBC 4.61 million/μg, Hb 14.2 g/dL, Hct 42.7%, platelets 117,000/μL, CRP 1.58 mg/dL, PT-INR 1.65, APTT 28.7 seconds, LDL 107 mg/dL, HDL 49 mg/dL, TG 63 mg/dL, T-chol 172 mg/dL, BNP 1755.6 pg/mL, cardiac troponin 201.5 pg/mL.

12-lead electrocardiogram (**Figure 1**): Heart rate 205 beats/min, ventricular tachycardia with right bundle branch block morphology and inferior axis.

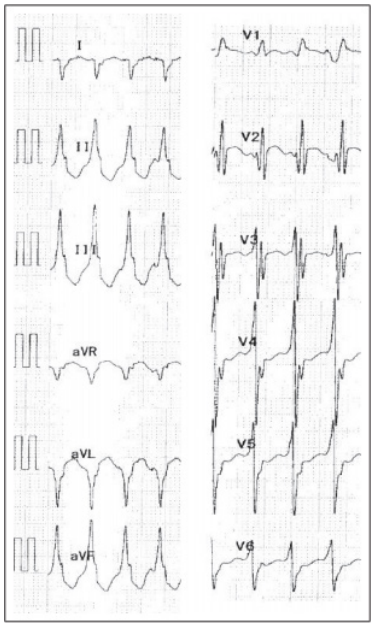

Figure 1. 12-lead electrocardiogram during tachycardia

Chest X-ray: Cardiothoracic ratio 52%, pulmonary congestion present.

Transthoracic echocardiogram on admission (performed during atrial fibrillation): Diffuse left ventricular wall motion abnormality, left ventricular ejection fraction 34%, left ventricular end-diastolic diameter 41.7 mm, left ventricular end-systolic diameter 35.0 mm, interventricular septum thickness 12.7 mm, left ventricular posterior wall thickness 10.0 mm, left atrial diameter 41.1 mm, mild mitral valve regurgitation present.

3. Clinical course

Acute heart failure due to ventricular tachycardia (VT) was diagnosed, and a plan for catheter ablation for VT was made. The obtained VT electrocardiogram (**Figure 1**) suggested an origin in the left ventricular outflow tract. Additionally, intermittent atrial fibrillation was concurrent, leading to a temporary state of heart failure requiring mechanical ventilation. However, when the heart failure symptoms stabilized, SMILIE was performed during atrial fibrillation, revealing a scar area in the left ventricular basal anterior septum (**Figure 2**).

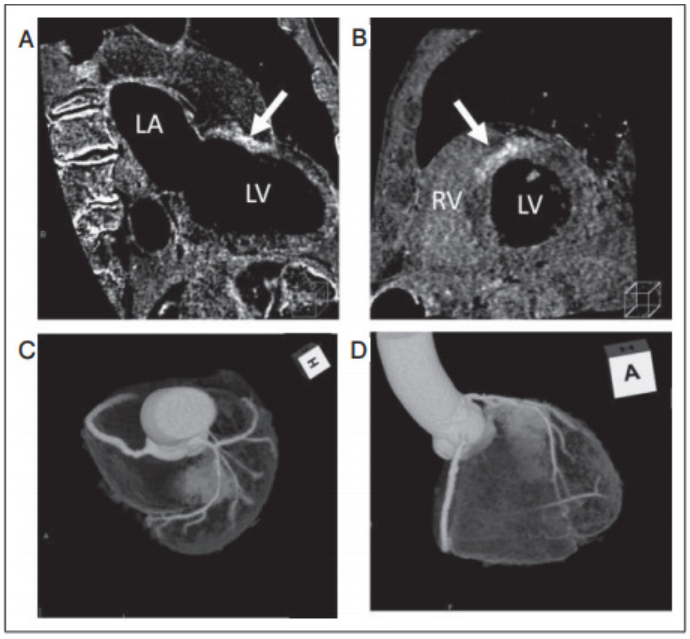

Figure 2. Cardiac CT: Late iodine enhancement (LIE) was observed in the left ventricular basal anterior septum. **(A)** Long axis; **(B)** Short axis showing LIE indicated by the arrow. Delayed enhancement is prominently observed on the ventricular septal side, suggesting the potential need for an approach from the right ventricular outflow tract; **(C)** Superior view of the 3D image of cardiac CT; **(D)** Right anterior oblique (RAO) view. LIE was observed in the left ventricular basal anterior septum.

Based on the scar area revealed by SMILIE and the electrocardiogram during tachycardia, mapping of the left ventricular outflow tract was deemed necessary. The scar area was predominantly located on the ventricular septal side, suggesting that an approach from the right ventricular side might also be necessary depending on the location of the earliest excitation site (**Figure 2**).

During catheter treatment, VT intermittently appeared and stopped from the beginning of the procedure, with a monomorphic pattern and a constant cycle length of 460 msec. Evaluating the tachycardia circuit with pace mapping or entrainment pacing was challenging due to atrial fibrillation and intermittent appearance of VT, which was expected to take time to determine whether pacing was capturing the ventricle.

With VT appearing and hemodynamics stable, a retrograde approach from the aorta was planned using

EnSite Precision™ and Advisor™ HD Grid catheters to evaluate the earliest excitation site of VT, primarily in the left ventricular outflow tract, by activation mapping within a short time. The earliest excitation site was identified in the left ventricular basal anterior septum, consistent with the scar site obtained with SMILIE (**Figure 3**). Voltage in the myocardium at the earliest excitation site was preserved. A potential preceding potential 25 ms ahead of QRS onset was observed at the earliest excitation site (**Figure 4**). Subsequently, when ablating at 40 W at the same site, VT ceased within 10 seconds of the initial ablation, and no further inducibility was observed, allowing completion of the procedure without complications with ablation only from the left ventricular side.

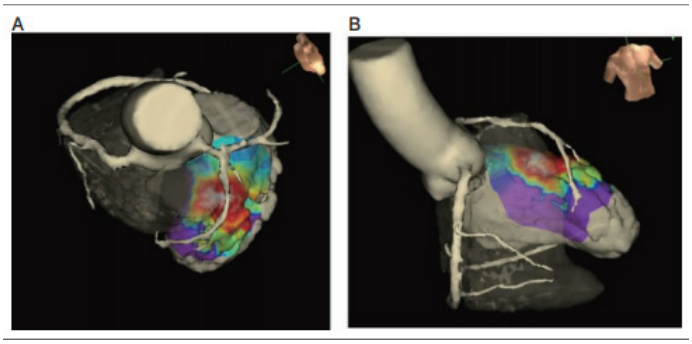

Figure 3. Activation map of ventricular tachycardia using a multi-electrode mapping catheter. **(A)** Superior view; **(B)** Right anterior oblique (RAO) view. The earliest excitation site was identified in the left ventricular basal anterior septum, consistent with the site of late iodine enhancement (LIE). The voltage at the earliest excitation site was relatively preserved.

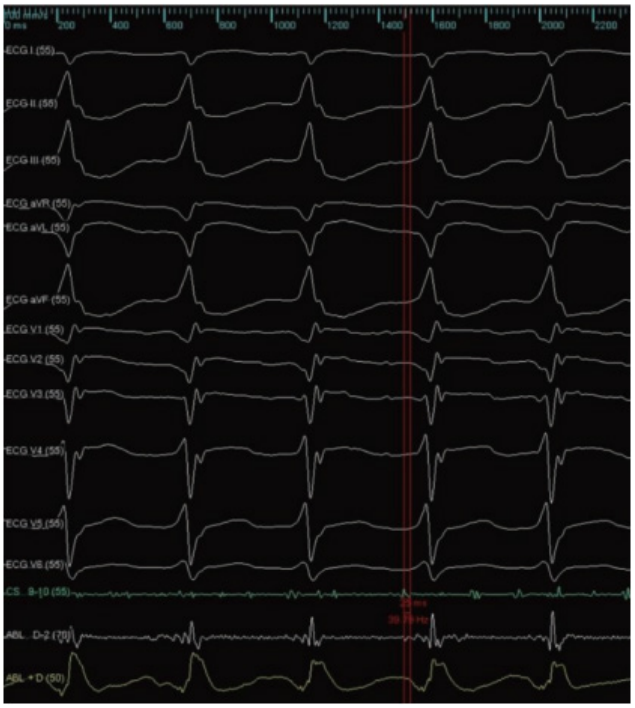

Figure 4. Intracardiac electrocardiogram during ventricular tachycardia before ablation initiation (EnSite Precision™). During ventricular tachycardia, atrial fibrillation persisted, and despite cardioversion attempts, it immediately recurred, rendering the tip potential of the ablation catheter unclear. At the earliest excitation site, a ventricular wave preceding the QRS onset by 25 ms was observed. When ablating at 40 W at the same site, ventricular tachycardia ceased within 10 seconds of the initial ablation, and no further inducibility was observed.

4. Discussion

In recent years, various innovations have been made to estimate the circuits of ventricular tachycardia (VT) with the advancement of technology. Verma et al. reported that the circuit of VT is often located at the border of scarred myocardium [7,8]. However, to delineate the scar border, mapping the entire left ventricle is necessary, which can prolong procedural time. Prolonged procedures in patients with reduced cardiac function are not recommended due to the risk of complications.

Additionally, the origin and circuits of VT are not confined solely to the endocardial or epicardial sides but may also involve the myocardial interior. However, current technologies do not allow mapping of the myocardial interior. Therefore, methods have been reported for extrapolating ablation based on VT maps [9]. Identifying the complex origins and circuits of VT within the patient's overall condition and limited treatment time is extremely challenging. Hence, attempts have been made to estimate VT circuits through imaging diagnostics pre-catheter ablation.

Currently, late gadolinium enhancement (LGE) in cardiac MRI is the standard method for delineating myocardial fibrosis and scar lesions, as mentioned in the "2016 Guidelines for the Diagnosis and Treatment of Cardiac Sarcoidosis" by the Japanese Circulation Society [10]. However, LGE has various limitations, including long imaging durations, low spatial resolution compared to CT, and difficulty in using the obtained images with 3D mapping systems for arrhythmia treatment. Late iodine enhancement (LIE) in cardiac CT also reflects myocardial fibrosis lesions [11,12], with reports suggesting its correlation with the origin of VT [13,14]. However, images obtained using this method often lack contrast and clarity, making it difficult to identify the origin and circuits of VT.

In this regard, a technique called Subtraction Myocardial Image for Late Iodine Enhancement (SMILIE) was utilized in this study. This novel method involves subtracting coronary phase images from delayed phase images to obtain delayed enhancement images (**Figure 5**). While previous reports have compared LIE-CT subtraction images with LGE images for myocardial ischemia assessment [15], the Japanese Red Cross Wakayama Medical Center's use of SMILIE with computed tomography angiography (CTA) potentially reduces radiation exposure and examination time compared to CT perfusion imaging, making it a more versatile imaging technique. With the advent of this method and 320-row Area Detector CT (Aquilion ONE/GENESIS Edition, Canon®), imaging the entire heart in one heartbeat has become possible regardless of arrhythmias or device presence, resulting in clearer contrast images compared to conventional LIE. Additionally, due to the clear contrast, information such as myocardial scarring in the myocardial interior, which was previously difficult to determine with catheter mapping, can now be discerned. This allows for pre-procedural planning of the approach method, contributing to the consideration of VT catheter treatment strategies.

Moreover, since the location of scar lesions can be predicted, it is possible to map only the area surrounding the scar lesions during catheter treatment. Furthermore, preoperative evaluation of coronary artery information and structures around the heart is also possible, contributing to the prevention of complications and reduction of procedural time. A comparison of features between delayed enhancement images obtained with SMILIE and those obtained with MRI is shown in **Table 1**. In this case, by estimating the approximate origin of VT from the 12-lead electrocardiogram during tachycardia and delayed enhancement sites obtained with SMILIE, successful elimination of VT was achieved with minimal mapping and ablation. As many VT cases occur in patients with reduced cardiac function, minimally invasive catheter treatment is required. This technique is extremely useful for VT catheter treatment as it allows pre-procedural clarification of information regarding myocardial fibrosis deep inside the heart. Furthermore, as it is an imaging technique, it is highly versatile and can be utilized in any facility with multi-row Area Detector CT.

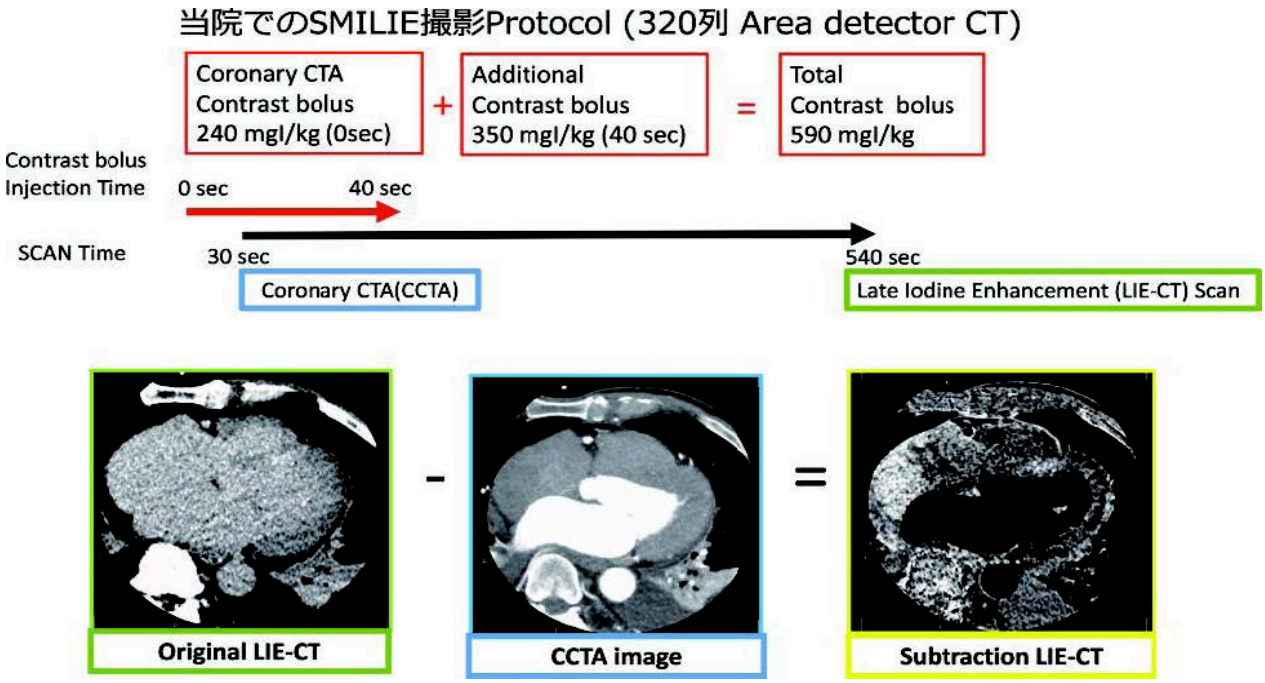

Figure 5. Imaging protocol for SMILIE at the Japanese Red Cross Wakayama Medical Center. The contrast agent is administered, and 30 seconds later, computed tomography angiography (CTA) of the coronary arteries and left atrium is performed. Approximately 9 minutes after contrast agent administration, delayed phase images of the left atrium are captured. SMILIE images are created by subtracting the CTA images from the delayed enhancement images.

Table 1. Comparison of features between SMILIE and LGE

	MRI (LGE)	CT (SMILIE)
Slice thickness	8–10 mm	0.5–1.0 mm
Examination time	Approximately 40–80 mins	Approximately 10 mins
Impact on renal function	Yes	Yes
3D-mapping system	Partial	Yes
Affected by arrhythmias	No	Yes
Feasible post-device insertion	No	Yes

Features of SMILIE

(1) Imaging with 320 rows allows for an extremely thin slice thickness of 0.5–1.0 mm, providing excellent spatial resolution.

(2) Short imaging time minimizes patient burden.

(3) Gadolinium cannot be used in dialysis patients, but iodine can be used.

(4) Obtained CT images can be directly incorporated into 3D-mapping systems for use.

(5) Imaging the entire heart in one heartbeat minimizes the influence of arrhythmias such as premature beats or atrial fibrillation.

(6) Imaging is easily feasible even in patients with inserted devices.

5. Conclusion

In this case, the delineation of scar sites obtained with SMILIE correlated very well with the earliest excitation sites of VT identified by the 3D mapping system. As a result, catheter treatment of VT was concluded in a short time without complications. The use of SMILIE in catheter treatment of VT is considered highly valuable for preoperative treatment strategy planning, higher success rate of procedures, reduction of procedural time, and complication prevention.

Disclosure statement

The authors declare no conflict of interest.

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Progress in the Study of Drugs for Thrombolytic Therapy of Acute Myocardial Infarction

Yayun Ling*

Chongqing Medical and Pharmaceutical College, Chongqing 401331, China

***Corresponding author:** Yayun Ling, hgg151313@126.com

Abstract: Acute myocardial infarction has become a serious disease that affects the quality of contemporary human survival, and improved efficacy and risk avoidance can be achieved through the upgrading of thrombolytic drugs and precise intervention. This article takes the development of three generations of thrombolytic drugs as the main line, and combs through the development of thrombolytic drugs from the era of urokinase and streptokinase to Alteplase and single-chain urokinase-type fibrinogen activator and their respective advantages and disadvantages. The advantages of three generations of tissue-type fibrinogen kinase derivatives, Reteplase, and tenecteplase, are compared and described in this article.

Keywords: Acute myocardial infarction; Thrombolytic therapy; Urokinase; Teneplase

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1. Introduction

Acute myocardial infarction belongs to the problem of cardiovascular blood supply disorders, which is classified as an acute and critical disease in cardiovascular medicine, and the priority of carrying out therapeutic interventions is higher, which needs to be realized as soon as possible to achieve effective interventions. Because the occurrence of this disease is more closely related to coronary atherosclerosis, when the hospital finds that patients have similar problems, it is necessary to carry out targeted measures promptly to help patients solve the problem [1]. With the continuous improvement of medical standards and the promotion of advanced treatment experience worldwide, the difficulty of treating acute myocardial infarction is decreasing, and the assessment of the actual type of acute myocardial infarction condition has been completed. According to the degree of occlusion of coronary artery thrombus, those completely close to occlusion are acute ST-segment elevation myocardial infarction, and the rest of the cases are categorized as non-ST-segment elevation myocardial infarction. According to relevant statistical data, the current myocardial infarction group is expanding, the incidence rate of rural middle-aged and elderly groups is increasing year by year, and the proportion of patients with ST-segment elevation type is getting bigger and bigger. Therefore, organizing the case data of patients with acute myocardial infarction, seeking more reliable treatment methods, and vigorously

carrying out research on thrombolytic therapy drugs are still the focus of current medical work.

Thrombolytic therapy is one of the recommended ways to solve coronary artery occlusion, which not only has a relatively long history of application and research but also has a more ideal practical application effect. It can open the relevant blood vessels, restore the blood supply to the patient's myocardial tissues promptly, lift the risk of death from ischemic heart disease, and together with percutaneous coronary intervention, emergency coronary artery bypass grafting and other techniques, form an emergency coronary artery embolism treatment plan to save the patient's life [2]. After nearly half a century of exploration, thrombolytic drugs have gone through many iterations and have accomplished three fruitful and significant changes, and have achieved the division of whether or not they act on fibrin (proteins), expanding the population for which thrombolytic drugs can be used to cope with, and pushing for a more diversified therapeutic approach. The important content of this article is to organize and summarize the existing research on thrombolytic drugs for acute myocardial infarction and complete a brief description of the relevant content as follows.

2. Mechanism of thrombolytic therapy for acute myocardial infarction

The work of the heart and the life activities of cardiomyocytes are dependent on blood transportation. When acute myocardial infarction occurs, the coronary arteries are basically in the situation of not being able to transport, at this time, the cardiomyocytes can only be maintained for no more than half an hour, and after that, they will be necrotic and lose their functions [3]. Once the degree of necrosis increases, it causes a regional chain reaction, an effect that is difficult to undo once it occurs, and a succession of life-threatening complications. According to the existing data show that in the coronary artery blockage will appear at several key time points, for example, at about 20 minutes, there will be necrotic cardiomyocytes; at more than 3 hours, myocardial cell necrosis will be more than half of the area; at more than 6 hours, cardiac myocardial tissue necrosis will be approximately 80%. Some scholars pointed out that when myocardial cell damage exceeds 40%, serious complications will begin to appear. The golden period of thrombolytic drug treatment in the infarction is within three hours; once the condition is delayed for more than three hours, the thrombolytic effect will be less than the expected results, but there is still a positive effect. Currently, some studies have also demonstrated the pain-relieving effect of thrombolytic therapy and found that even in patients with severe myocardial infarction, the adverse effects can still be reduced by thrombolytic therapy.

3. Thrombolytic therapy for acute myocardial infarction

Some studies have indicated that in the case of appropriate intervention methods, the thrombolytic time window of the patient will be expanded, which is more conducive to the recovery of the patient. Therefore, when carrying out thrombolytic drug therapy, it is necessary to flexibly use thrombolytic therapy to play the best therapeutic effect according to the situation. Intravenous thrombolytic therapy is the most common. According to the relevant research comparative report, intravenous thrombolytic therapy has obvious advantages, simple operation, and high acceptance by patients, so thrombolytic therapy is widely promoted. It mainly uses the upper limb channel as a medium to add thrombolytic drugs into the patient's blood circulation to achieve the effect of dissolving the thrombus. Secondly, arterial thrombolysis is relatively complex. The process is accomplished with the aid of direct imaging. The principle is to utilize a multilaterally perforated thrombolytic catheter to directly dissolve the thrombus. Studies have shown that this method is precise, less harmful, more targeted, and has a relatively high rate of revascularization, and intracoronary thrombolysis is one of the more effective types [4]. However, regardless of thrombolytic treatment methods, attention to the thrombolytic catheter

location, drug dose, and other key issues are required to maximize the control of bleeding risk.

4. Thrombolytic drug research

Research on thrombolytic drugs begins with understanding the composition of thrombus. Acute myocardial infarction patients' thrombus is generally composed of fibrin and other substances, and relevant studies have shown that dissolving fibrin can better complete the blood vessel opening. Therefore, most thrombolytic drugs follow the basic principle of activating fibrous enzymes to degrade fibrin. However, it is difficult to standardize the physical condition of patients, and it is impossible to achieve standardized treatment, so non-specific fibrinogen activators and specific fibrinogen activators are needed to cope with different conditions.

4.1. First-generation thrombolytic drugs

The first generation of thrombolytic drugs all belong to the non-specific fibrinogen activator fluid, whose important branches are two kinds of urokinase and streptokinase. Urokinase is a synthetic drug substance, which is named urokinase because it needs to be extracted with the help of urine or related tissue fluids to extract the necessary double-chain serine protease. According to research reports, it stimulates the thrombolytic zymogen in the blood, accelerates its conversion and functioning, and the substance has a certain antithrombotic coagulation effect, which partially facilitates the elimination of blood clots and accelerates the therapeutic process. The results of its use show that the drug is not targeted by the body as an antigen, the loss of potency and safety are guaranteed. As a more targeted drug, it also has the property of low cost, which was once chosen and sought after by the market. However, with the expansion of the scale of use, the drug gradually reflected the shortcomings of non-specific fibrinogen, that is, consuming excess fibrin, resulting in bleeding symptoms. Therefore, when using generation urokinase for treatment, it is required to try to maintain in the appropriate window period, intravenous thrombolysis not more than 6h, and need to confirm the status of the blood vessel after stopping the drug, to observe the effect, to prevent re-occlusion, and also need to control the time of drug use, to avoid the danger. Relevant research data show that with the improvement of pharmacological management, personnel quality, and other objective factors, as well as the reasonable improvement of urokinase, patients receiving urokinase after the vascular recanalization rate, from about 70% to nearly 83%; bleeding and other adverse conditions statistics are also reduced from more than 10%, and the overall quality of treatment continues to improve [5].

Streptokinase is an effective thrombolytic substance extracted from the culture fluid of hemolytic streptococci, and according to the results of the controlled study, it is pointed out that the drug, as non-specific fibrinogen activating fluid, has a similar action effect to streptokinase, and the manufacturing cost meets the market requirements, but the generalization of this drug is relatively poor in comparison with that of urokinase because the probability of this drug being regarded as an antigen by the human body during its use is that it will cause allergy, fever, and the safety coefficient is relatively low, hence leading to rare utilization of this drug in current clinical practice.

4.2. Second-generation thrombolytic drugs

The manufacture of second-generation thrombolytic drugs cannot be separated from the progress of related genetic engineering technology. To upgrade and improve the drug to avoid complications caused by non-specific thrombolytic zymogen, the type of second-generation drug is mainly a tissue-type fibrinogen activator that can complete specific thrombolysis. A representative one is Alteplase. The therapeutic effect of this drug relies on the 527 amino acids it carries, and in actual treatment, it can selectively activate the fibrinogen in the

thrombus to break down the fibrin in the thrombus and complete thrombolytic treatment. The specificity of the drug can help patients eliminate the risk of systemic fibrinolysis. Because the drug has a relatively short half-life, the effect is not sufficiently sustained. During application, Alteplase is used in relatively large doses and requires the completion of short periods of administration of large quantities of the drug. Relevant institutions recommend the use of intravenous thrombolysis, according to 15 mg, 20 mg, and 35 mg gradient injection, and according to the actual situation to control the dosing interval. Authoritative organizations on the drug dosage of the control demonstration concluded that the dose halved, but the efficacy of the difference is not obvious. However, compared with the first generation of drugs, in the second generation of drugs, the thrombolytic recanalization rate increased significantly, the mortality rate decreased to less than 1.2%, and the reinfarction rate after the realization of segmental administration was significantly lower than that of the first generation of drugs [6,7]. At the same time, some studies have emphasized the possibility of alteplase to prevent microvascular re-occlusion and put forward related ideas, but the practical verification of this idea is still divided.

Single-chain urokinase-type fibrinogen activators are representative of the better-performing second-generation agents. It has a relatively small number of amino acids and retains the dual properties of zymogen and enzyme. These properties allow it to perform thrombolysis in a way that ensures that the thrombus is dissolved relatively completely and that the fibrin in the plasma is not affected. Bleeding is relatively low and patients are less likely to develop allergic reactions. Studies have demonstrated the safety and efficacy of this drug.

4.3. Third-generation thrombolytic drugs

The main types of third-generation drugs are tissue-type fibrinogen kinase derivatives, of which Reteplase and Teneplase are used relatively frequently.

Reteplase itself is a genetically engineered and retooled derivative of Alteplase. Reteplase retains the potent effect of thrombolysis while reducing its specific receptor-binding properties through modified amino acid fragments to fully extend the drug's half-life cycle and improve therapeutic efficacy. It should be noted that Reteplase requires continuation of intravenous access and is used alone. Mixed administration with other drugs is prone to unpredictable trouble. Foreign research comparing Reteplase and Alteplase efficacy showed that the observation group of Reteplase had superior effectiveness, showing higher blood flow levels and significantly lower vascular re-infarction rates as compared to the observation group of Alteplase. Several medical institutions have given positive comments on this new type of drug [8,9].

Teneplase is a mutation product, as its effectiveness prolongation relies on multiple point mutations to achieve. According to relevant research, Teneplase not only prolongs the half-life cycle to 11–20 minutes but also has a nearly 14-fold enhancement of its fibrin specificity [10]. Both laboratory results and statistical data from medical unit studies demonstrated the superiority of Teneplase. Comparative results also found that when Teneplase was used in elderly female patients, it was able to reduce the incidence of cerebral hemorrhage and reduce blood transfusions. Additionally, the drug can realize thrombolysis through a single intravenous injection, which is more timely and convenient for acute patients. At present, China's production of Teneplase has been listed and put into use, and all the experimental data are relatively excellent. In the application field of elderly patients, the research of this drug is being supplemented, but there have been experiments to prove that after halving the dose, the safety and effectiveness of the drug are worth recognizing. However, the clinical aspect should continue to promote thrombolytic drug research, which will further amplify the therapeutic effect.

5. Conclusion

In summary, the continuous evolution of third-generation drugs has improved the effectiveness and safety of thrombolytic therapy, allowing patients to better cope with acute myocardial infarction. Moreover, the use of third-generation drugs has become the mainstream of treatment, the prolongation of its half-life is convenient for patient treatment, and the maintenance of specificity makes thrombolytic therapy more targeted. However, the clinical side should continue to optimize the treatment process, refine the details of drug therapy, more targeted control of drug dosage and timing, and rationally deal with the prognosis of the risk, thereby further enhancing the therapeutic efficacy of the drug itself and eliminating acute myocardial infarction issues in patients.

Disclosure statement

The author declares no conflict of interest.

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Prognostic Value of Cardiac Color Doppler Ultrasound in Patients with Chronic Heart Failure

Meidi Zhu, Lingling Hua, Yu Zou, Puyi Xiang*

Xishan People's Hospital of Wuxi City, Wuxi 214105, Jiangsu Province, China

***Corresponding author:** Puyi Xiang, zhumeidi1979@163.com

Abstract: *Objective:* To investigate the value of cardiac color Doppler ultrasound (CDUS) in determining the clinical characteristics and assessing the prognosis of patients with chronic heart failure (CHF). *Methods:* 200 patients with CHF admitted to our hospital from January 2021 to June 2023 were selected as the study subjects, and these 200 patients were followed up for 6 months, with 159 cases in the surviving group and 41 cases in the deceased group, and examined with a diagnostic CDUS instrument (model GEVividE95ACUSONSC2000). The detection rate of chronic heart failure and cardiac function indexes of the two groups were observed. *Results:* The deceased group showed a chronic heart failure detection rate of 92.68%, which was significantly higher than the surviving group (76.73%; $P < 0.05$). Moreover, the cardiac function indexes of both groups were significantly different ($P < 0.05$). *Conclusion:* By performing cardiac ultrasonography on patients with CHF, their cardiac function can be clearly understood and the changes can be timely detected during treatment, hence physicians can formulate a more reasonable treatment plan for patients and improve their quality of life.

Keywords: Cardiac color Doppler ultrasound; Chronic heart failure; Prognosis; Detection rate

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1. Introduction

Chronic heart failure (CHF) is a group of clinical syndromes caused by a variety of heart diseases and characterized by stagnation of the pulmonary and/or physical circulation, resulting in damage to the myocardium and/or a decline in its function, which is unable to meet the needs of the body's daily activities, and cardiac distress and dyspnea are the most common symptoms of patients with CHF, and an important indication for patients to seek medical attention [1]. However, due to the relatively late development of cardiac Doppler technology, some patients do not receive cardiac ultrasound examinations in time, thus missing the best time for treatment [2,3]. Chronic heart failure is associated with a variety of factors, such as changes in myocardial structure and function, and chronic heart failure reduces the pumping capacity of the ventricles after filling, reduces the amount of heart output per beat, and impairs the heart's function, which has a serious impact

on the patient's physical and mental health. Early symptoms of chronic heart failure lack specificity, and the accuracy of diagnosis at this time is not high, which can lead to a delay in the best treatment time. Therefore, it is of great clinical value to effectively evaluate CHF patients at the early diagnostic stage to understand their disease progression and prognosis. In recent years, with the continuous progress of ultrasound imaging technology, cardiac ultrasound, as a noninvasive, convenient, and fast detection means, has been widely used in the diagnosis and treatment of cardiovascular diseases [4,5]. In this study, the value of cardiac ultrasound in evaluating the prognosis of patients with CHF was explored by performing ultrasonography on patients with chronic heart failure, comparing the detection rate of chronic heart failure and cardiac function indexes in the survival group and the death group after 6 months of follow-up, to provide a reliable basis for the clinic.

2. Materials and methods

2.1. General information

The 200 CHF patients admitted to the Xishan People's Hospital of Wuxi City from January 2021 to June 2023 were selected as the study subjects, among which 125 were male patients and 75 were female patients, aged 37–79 years, with an average age of 64.21±8.53 years, and these 200 patients were followed up for 6 months, with 159 cases in the surviving group and 41 cases in the deceased group. There were 104 males and 55 females in the surviving group, aged 38–73 years, with an average age of 65.36±8.24 years, while 21 males and 20 females in the deceased group, aged 37–79 years, with an average age of 66.16±8.89 years, and there was no statistically significant difference in the general data of gender and age between the two groups ($P > 0.05$). The value of cardiac color Doppler ultrasound in assessing the prognosis of patients with chronic heart failure

Inclusion criteria: (1) Patients have been clinically diagnosed with chronic heart failure and meet the relevant diagnostic criteria; (2) Patients should be 18 years old and above, with no upper age limit; (3) According to the cardiac function classification standard of the New York Heart Association (NYHA), patients' cardiac function should be in the range of II-IV; (4) the cardiac color Doppler ultrasound images are clear, which can accurately assess the structure and function of the heart; (5) patients or their legal representatives should sign an informed consent to participate in this study; (6) patients should have the conditions for long-term follow-up, including stable residence and contact information. The patients or their legal representatives should sign an informed consent form to participate in the study; the patients should have the conditions for long-term follow-up, including stable residence and unobstructed contact information.

Exclusion criteria: (1) Patients are in acute heart failure episodes or have a recent history of acute heart failure episodes; (2) Patients have severe valvular disease, such as rheumatic heart disease, congenital valvular anomalies, etc.; (3) Patients have a history of previous cardiac surgery, such as cardiac valve replacement, cardiac transplantation, etc.; (4) Patients suffer from active malignant tumors or have a life expectancy of less than one year; (5) Patients have severe hepatic or renal insufficiency, which may affect the cardiac function and prognosis; (5) Patients with severe mental disorders that prevent them from cooperating with the study or providing accurate follow-up information; (6) Female patients who are pregnant or breastfeeding; (7) Patients with known hypersensitivity to ultrasound contrast agents.

2.2. Methods

Color ultrasound diagnostic instrument (instrument model: GEVividE95ACUSONSC2000) was used for the examination, the probe frequency was 3.5 MHz, and the apical four-chamber view was taken to observe the cardiac structure and size changes when the body position was left-lateral recumbency or right-lateral recumbency. The patient's heart rate was used as a reference index, and the patient was kept in a quiet state,

then the measurement and recording of ultrasound parameters began. Cardiac function was evaluated by the following parameters: left ventricular ejection fraction (LVEF; %), left ventricular end-diastolic internal diameter (LVIDd; mm), and left ventricular end-systolic internal diameter (LVIDs; mm).

2.3. Observation indicators

Detection rates of chronic heart failure and cardiac function indexes of the two groups were recorded. Positive diagnostic criteria included LVEF of less than 50%, LVIDd of more than 55 mm, and LVIDs of more than 40 mm.

2.4. Statistical analysis

The results of the study were imported into SPSS 22.0 software to analyze the data. Count data were expressed as percentages, and the χ^2 test was used for comparison between groups. Measurement information was expressed as mean ± standard deviation (SD), and a *t*-test was used for comparison between groups. The result difference was considered significant at $P < 0.05$.

3. Results

3.1. Detection rate

The detection rate of chronic heart failure was higher in patients in the deceased group as compared to the surviving group ($P < 0.05$), as shown in **Table 1**.

Table 1. Comparison of detection rates between the two groups

Group	Number of examples	Number of cases detected	Detection rate
Deceased Group	41	38	92.68
Surviving Group	159	122	76.73
χ^2			5.145
P			0.023

3.2. Indicators of cardiac function

The data of the cardiac function indexes of the patients in the surviving group differed from those of the deceased group ($P < 0.05$), as shown in **Table 2**.

Table 2. Comparison of cardiac function indices in the two groups

Group	Number of examples	LVEF (%)	LVIDd (mm)	LVIDs (mm)
Deceased Group	41	37.62 ± 3.78	55.57 ± 5.43	47.68 ± 5.07
Survival Group	159	60.49 ± 8.13	40.56 ± 4.11	21.06 ± 4.14
t		17.506	19.438	34.986
P		0.000	0.000	0.000

4. Discussion

CHF is a group of clinical syndromes caused by myocardial hypocontractility and/or increased cardiac filling pressure, resulting in ventricular filling or blood return obstruction [6]. In China, the incidence of CHF shows a trend of youthfulness, and the incidence is increasing with the development of the social economy and the

aging of the population. Heart failure is one of the most common complications in the late stages of coronary heart disease, hypertension, and other diseases, seriously threatening the life and health of patients. Therefore, early diagnosis and timely treatment of CHF patients are very necessary. Cardiac ultrasound can provide cardiologists with accurate and reliable information to help clinicians determine the condition of patients and formulate appropriate treatment plans, which is of great clinical value. By comparing the clinical characteristics and prognosis of the two groups of patients, we found that cardiac ultrasound has a certain application value in the prognostic assessment of CHF patients, which can help to improve the prognosis of patients.

The results of this study showed that the detection rate of chronic heart failure in the deceased group was 92.68%, which was higher than the surviving group of 76.73% ($P < 0.05$). This indicates that cardiac ultrasound has a significant detection rate of chronic heart failure in patients with CHF and that the adoption of active and effective therapeutic measures can effectively improve the quality of life of the patients. At the same time, the cardiac function indexes of patients in the surviving group were different from those of the deceased group ($P < 0.05$), and echocardiographic indexes have a certain reference value in the prognostic evaluation of CHF patients. Cardiac color Doppler ultrasound, as a noninvasive imaging method, demonstrated its unique effect in assessing the prognosis of patients with CHF.

Xie *et al*. [7] found that cardiac color Doppler ultrasound can accurately assess the patient's heart size, ventricular wall thickness, ventricular chamber size, and other morphological indicators, which can provide a basis for determining cardiac function and prognosis. Doppler technology can assess the systolic and diastolic function of the heart, including ejection fraction, ventricular filling velocity, and other indicators, which are essential for predicting the prognosis of patients with chronic heart failure. The monitoring of blood flow velocity and direction can assess the kinetic status of blood flow in the heart, such as the blood flow velocity and regurgitation of the mitral valve and aortic valve, which can help determine the degree of impairment of cardiac function and prognosis. Color Doppler ultrasound of the heart can also indirectly assess the changes in intracardiac pressure, such as the pulmonary artery pressure and the end-diastolic pressure of the left ventricle, which can provide references to assess the prognosis of the patients. Lu *et al*. [8] found that ultrasound can detect myocardial lesions, such as myocardial hypertrophy, myocardial thinning, etc., which helps to reveal the etiology and pathophysiological process of chronic heart failure, valvular lesions are one of the common causes of chronic heart failure, and ultrasound can accurately identify valvular stenosis, closure insufficiency, etc., which can provide a basis for the choice of treatment and prognosis assessment, and cardiac color Doppler ultrasound can be used to monitor the patient's response to response to treatment, such as drug therapy, cardiac resynchronization therapy, etc., which helps to adjust the treatment plan and optimize the prognosis. Through regular ultrasound examination, the progress and regression of patients' conditions can be monitored, providing important information for clinical decision-making. Kang *et al*. [9] found that the combination of ultrasound indexes and other clinical information can be used to risk-stratify patients, identify high-risk and low-risk patients, and provide a basis for the development of personalized treatment strategies and prognosis prediction. Through regular cardiac color Doppler ultrasound examination, the treatment effect and prognosis improvement of patients can be assessed. For example, indicators such as the improvement of ejection fraction and the slowing down of ventricular enlargement after treatment indicate that the treatment is effective and the prognosis of patients is expected to improve. Cardiac color Doppler ultrasonography has a high degree of operability and reproducibility, which makes it of practical value in the prognostic assessment of patients with chronic heart failure.

In summary, cardiac ultrasound examination of CHF patients can provide a clear understanding of their cardiac function and timely detection of changes in their condition during treatment, as well as the development

of a more reasonable treatment plan for patients to improve their quality of life. By accurately evaluating cardiac structure, function, and hemodynamic parameters, and monitoring changes in the condition, it provides an important basis for clinical decision-making and helps to optimize patient treatment and prognosis management. However, ultrasound technology has certain limitations and is not able to clearly observe important information such as heartbeat and blood flow, so it is not able to make accurate judgments on some congenital heart diseases, heart valve diseases, and myocardial infarction. In addition, the lack of precision in ultrasound diagnosis may lead to missed or misdiagnosis, resulting in delayed or aggravated conditions.

No correlation between heart rate and prognosis was observed in this study, probably due to the use of diagnostic color ultrasound, which has relatively high detection data. Some studies have shown that the systolic anterior wall myocardial resistance index (ECRI) and the right ventricular end-diastolic volume/left ventricular end-diastolic volume ratio (RV/LV ratio) can be used as independent risk factors for determining the mortality rate in patients with chronic heart failure [10]. ECRI can be used to predict cardiac death, but its role in chronic heart failure is unclear. In addition, this study only assessed LVEF, LVIDd, LVIDs, and survival rate, which lacks the assessment of other indexes such as level of cardiac function, hemodynamic index, and atrial size. Therefore, it is necessary to further expand the sample size for analysis. Although cardiac ultrasound is now commonly used in clinical practice to diagnose CHF and to adjust the treatment plan according to its results, the accuracy of ultrasound diagnosis still needs to be improved.

Disclosure statement

The authors declare no conflict of interest.

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A Case of Cone Reconstruction and Aortic Valve Replacement for an Adult Patient Diagnosed with Ebstein's Anomaly Incidentally during Preoperative Examination of Severe Aortic Regurgitation – A Secondary Publication

Hiroki Sunadoi[1]*, Noriyoshi Ebuoka[2], Masato Fusegawa[1], Hidetsugu Asai[2], Takashi Sugiki[1], Yutaka Makino[1]

[1]Department of Cardiovascular Surgery, Oji General Hospital, Tomakomai, Japan
[2]Department of Congenital Cardiovascular Surgery, Hokkaido Medical Center for Child Health and Rehabilitation, Sapporo, Japan

***Corresponding author:** Hiroki Sunadoi, h.sunadoi@me.com

Abstract: Recently, there have been some reports that cone reconstruction can be performed in the repair of Ebstein's anomaly with acceptable results on a child. On an adult with Ebstein's anomaly, optimal surgical indication and choice of the operative procedure are controversial. A man in his seventies was diagnosed with Ebstein's anomaly incidentally during the preoperative examination of severe aortic regurgitation. We performed aortic valve replacement and cone reconstruction because his tricuspid regurgitation was moderate. There was no severe complication and he was discharged. No sign of recurrence has been observed after 4 months of follow-up. We present a case in which cone reconstruction and aortic valve replacement were successfully performed on an adult patient diagnosed with Ebstein's anomaly and severe aortic regurgitation.

Keywords: Ebstein's anomaly; Cone reconstruction; aortic valve replacement

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1. Case study

A 70-year-old male had a complaint of difficulty breathing and swelling of his lower legs. He has a family history of his father and brother suffering from stroke, and a history of neurologic syndrome, Sugamo segmental sclerosis, hypertension, and hyperlipidemia.

The patient was followed up for aortic regurgitation (AR) by his primary care physician but was referred to the Department of Cardiology because of gradually progressive dyspnea and worsening leg edema. The patient

was admitted to the hospital with a diagnosis of renal failure and heart failure. Ultrasonography revealed severe AR and moderate tricuspid regurgitation (TR). The cause of TR was found to be deviation of the septal apex toward the apex of the heart, and a diagnosis of Ebstein's disease was made. After induction of dialysis, the patient underwent surgery.

On admission, he was 158.6 cm tall, weighed 57.1 kg, NYHA grade I, SpO_2 97% (room air), and had a clear breath sound on auscultation with a diastolic heart murmur of Levine 2/6 at the left border of the sternum. The abdomen was flat and soft with bilateral leg edema.

An electrocardiogram showed that the patient was in sinus rhythm with a heart rate of 61 beats/min, a PR interval of 224 ms, first-degree atrioventricular block, RV5 + SV1 of 5.03 mV, and left ventricular hypertrophy. There was no evidence of leg block or axial deviation.

Radiographs showed that the heart was enlarged with a cardiothoracic ratio of 67.2%, and the right first and second arches protruded (**Figure 1**). The diaphragmatic angles of the ribs were bilaterally acute, and there was no evidence of pulmonary congestion.

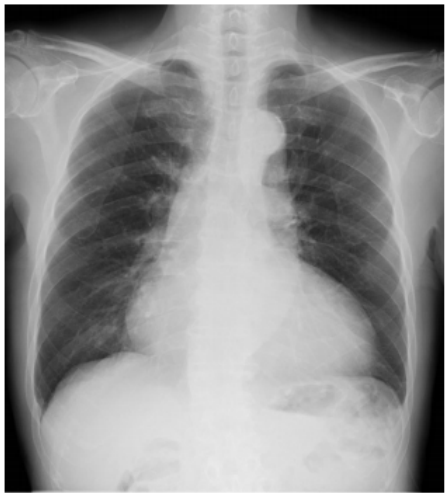

Figure 1. Preoperative chest X-ray with cardiothoracic ratio of 67.2%

The contrast-enhanced computed tomography (CT) showed that in addition to the calcification of the aortic valve and its surroundings, small and large calcifications were scattered throughout the aorta from the arch to the common iliac artery bifurcation. The diameter of the ascending aorta was 32 mm, and the peripheral aorta was within normal limits.

The transthoracic echocardiography (TTE) revealed a left ventricular ejection fraction (EF) of 58%, mild left ventricular wall thickening, and good wall motion. The aortic valve was calcified at the bicuspid apex, and moderate to severe AR was observed.TR was moderate, regurgitation velocity was 2.6 m/s (pressure gradient 26 mmHg), and tricuspid annulus diameter was 39.8 mm. The patient was diagnosed with Ebstein's disease and Carpentier type A. The Celermajorindex was 0.28, and the right ventricular wall motion was good (**Figure 2**). The mitral and pulmonary valves were abnormal. The mitral and pulmonary valves were normal. There was no interatrial traffic.

The patient had a severe AR with episodes of heart failure, and the decision was made to perform a large artery valvotomy. The patient was judged to be a candidate for surgery. The patient underwent surgery for the tricuspid valve. If the intraoperative findings showed mild plastering, he underwent valvuloplasty alone to control TR, otherwise, he underwent cone surgery.

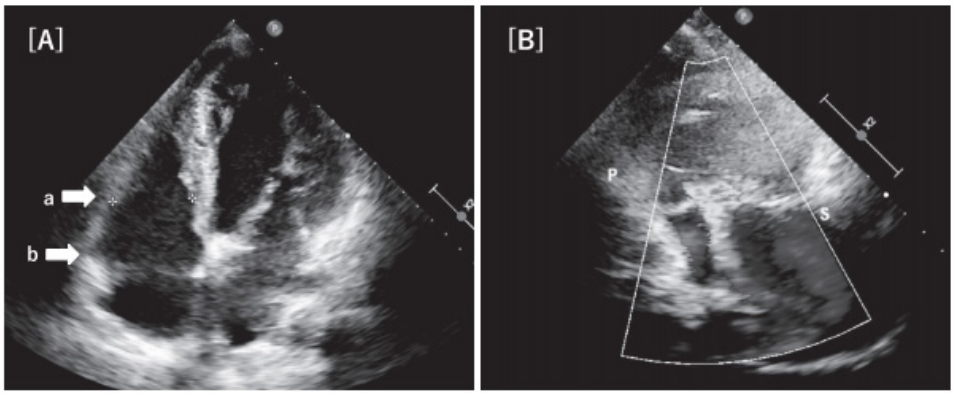

Figure 2. Preoperative transthoracic echocardiography. **(A)** In the four-chamber view, arrow a points to the functional tricuspid annulus, and arrow b points to the anatomical tricuspid annulus. Celermajor index = 0.28. **(B)** In the apical 2-chamber view, S is the septal leaflet, and P is the posterior leaflet. TR moderate.

1.1. Surgical intervention

The patient was placed in a supine position, ventilator-controlled, and under general anesthesia. The patient was approached through a median sternotomy, and extracorporeal circulation was established through the ascending aorta for blood supply and the superior and inferior vena cava for deblooding. A vent tube was inserted through the right superior pulmonary vein, and myocardial protection was provided by selective progressive and retrograde coronary perfusion.

Observation of the tricuspid valve after cardiac arrest reveals that the anterior apex is approximately 1/2 of the posterior apex. After cardiac arrest, the tricuspid valve was observed to be plastering extensively on the posterior half of the anterior apex, the posterior apex, and the septal apex. The anterior apex of the tricuspid valve was plastering over a wide area. The septal apex was not plastering. Because the plastering was not localized at the septal apex, regurgitation control was not possible by valve ring suture alone. The patient underwent Cone surgery as planned. The tricuspid valve ring was determined from its coloration, and the inner side of the ring was incised with a scalpel clockwise from the anterior to the posterior apex. The valve was detached from the right ventricular myocardium with a scalpel and shears, and all but the primary chordae were removed. Because the plastering right ventricular myocardium on the septal apex side and septal apex of the posterior apex was very thin and partially defective, the dissection was limited to about 2/3 of the posterior apex (**Figure 3**). The posterior apex was incised longitudinally from the valve ring to the apex, and the anterior septal commissure of the septal apex was incised longitudinally as well, and the severed ends were sutured with 5-0 monofilament thread to form a cone shape. Contralateral to the coronary sinus, the anatomic tricuspid valve ring was sutured with a 2-0 prejet polyester suture to the circumference of the cone, and the right atrialized right ventricle was subsequently longitudinally plicated. Because the valve ring was not histologically fragile, the Cone was pulled up over the sutured anatomic tricuspid valve ring and sutured directly and continuously with 5-0 monofilament thread. No regurgitation was observed during the water test. The aortic valve was tricuspid with minimal degeneration or calcification. The valve leaflets were resected and sutured with Inspiris RESILIA 23 mm (Edwards Lifesciences Irvine, California) using a 2-0 polyester suture with a single nodal suture. The patient was easily removed from the heart-lung machine. The operative time was 4 hours and 44 minutes, the ventilatory time was 3 hours and 6 minutes, and the aortic disconnection time was 2 hours and 27 minutes.

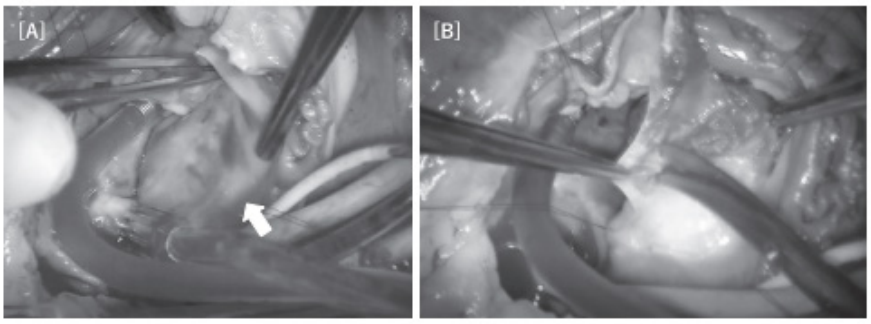

Figure 3. Intraoperative view. **(A)** The posterior leaflet was extensively plastered (arrow). **(B)** Anterior and posterior leaflets were detached. It was difficult to detach the whole posterior leaflet because of the thin right ventricular myocardium.

1.2. Postoperative course

The patient was intubated and sent to the intensive care unit. The patient was weaned from the ventilator on the first postoperative day. The patient was transferred to the general ward on postoperative day 2. Postoperative TTE on postoperative day 7 showed EF 55%, no cardiac depression, no AR, and mild TR. Immediately after surgery, the patient had occasional atrioventricular junction (AVJ)-like waveforms, but they gradually improved. The patient was discharged from the hospital on the 21st postoperative day.TTE was performed again on the 31st postoperative day, and TR was observed trivially to mildly along the septum between the anterior apex and septal apex, regurgitation velocity improved to 1.9 m/s (pressure gradient 14 mmHg), tricuspid valve ring diameter was 27.4 mm, and there was no obvious tricuspid stenosis (TS). The tricuspid valve ring diameter was 27.4 mm. Four months after surgery, the patient has been an outpatient without any significant changes (**Figure 4**).

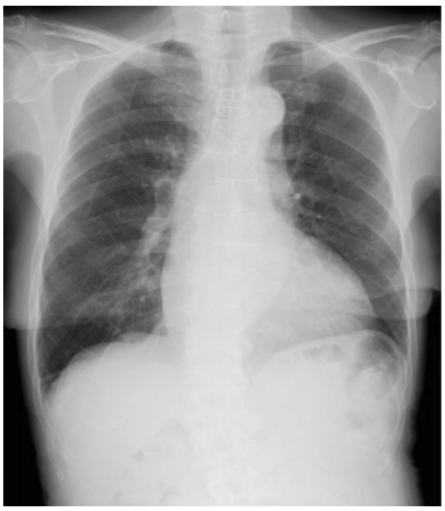

Figure 4. Postoperative chest X-ray with a cardiothoracic ratio of 56.2%

2. Consideration

Ebstein's disease, first described by Wilhelm Ebstein in 1866, is an uncommon disease caused by abnormal development of the tricuspid valve and right ventricle with a frequency of less than 1% of congenital heart disease (1 in 200,000 births).

The disease is characterized by a lack of delamination of the tricuspid valve septal apex and posterior apex

in the right ventricular wall, a functional valve ring shifted toward the apex, right ventricular enlargement and thinning (right atrialization), anterior apex deformation, and right ventricular dysfunction due to narrowing, which may present in a variety of combinations and degrees [1,2]. According to Watson's analysis of 505 cases, 71% of patients aged 1–25 years and 60% of patients aged 25 years or older were in NYHA I-II with no major limitations in daily life [3]. In a study of 202 cases by Celermajor *et al*., cyanosis and heart failure were the main symptoms in neonates and infants, while relatively mild symptoms such as heart murmurs and arrhythmias were more common in childhood and adulthood, and the annual mortality rate was 36% in the first year from birth to age 1, compared with 1.4% between 10 and 40 years of age [4]. The prognosis for Ebstein's disease, which does not require intervention until adulthood, is not so bad. Regarding the indications for surgery for Ebstein's disease in adulthood, Japanese guidelines for adult congenital heart disease and European guidelines recommend surgical intervention in patients with symptomatic or laboratory signs of right heart failure. In fact, the Mayo Clinic operated on 81 patients with Ebstein's disease aged 50 years or older between 1980 and 2010, of whom 85% were operated on in NYHA III-IV cases, and reported a relatively good 10-year survival rate of 71%.

In the report, the authors also suggested that early surgical intervention may be considered because of the poor prognosis in patients who underwent surgery at an advanced age or who did not show improvement in NYHA after surgery [5].

In the surgical treatment of simple Ebstein's disease after infancy, the cone procedure reported by da Silva et al. in 2007 has attracted much attention because, unlike the conventional technique of mono-cusp repair, this technique creates a new conical valve with complete dissection of almost all valve leaflets, which allows for diastolic central flow and better anatomy. This technique is considered to be a more anatomical repair, as it allows for central flow during diastole.

In the report, Cone surgery was performed in 40 patients, and the TR grade improved from 3.6 ± 0.5 to 1.2 ± 0.5 with no valve replacement at an average of 4 years of observation [6]. The choice between tricuspid valve repair or replacement in cases requiring surgical intervention in adulthood is still a matter of debate, but there are increasing reports of cone surgery being used as the surgical choice for tricuspid valve replacement [7,8]. Ozbek *et al*. compared cone surgery with other tricuspid valve procedures in adults with Ebstein's disease aged 20 years or older, with an average age of 44 years, and reported that cone surgery was superior in various aspects such as shutdown time, ICU stay time, hospital stay time, and TR survival, and cone surgery had no perioperative mortality [9]. Cone surgery was superior in various aspects, such as time of interception, ICU stay, length of hospital stay, and survival of TR.

In this case, Ebstein's disease was found incidentally during a close examination of the AR, and although the TR was moderate, we decided to intervene at the same time as AR surgery. Preoperative examination revealed relatively mild Ebstein's disease, and considering the patient's age and other factors, we assumed that TR could be controlled by valvuloplasty alone, but actual observation revealed extensive plastering. However, the plastering was extensive, and the intervention of the tricuspid valve in this case was very significant. The patient was treated with a cone procedure, which was a preferable alternative to a prosthetic valve because the patient was on hemodialysis. However, in this case, the patient was prepared for bioprosthetic valve replacement, but if the available valve leaflets are limited or TS is suspected during the intraoperative TEE evaluation, switching to tricuspid valve replacement should be considered.

Regarding surgical intervention for simple TR associated with left heart surgery other than tricuspid valve surgery, aggressive simultaneous surgery may be considered even if the patient has moderate TR at risk [10]. As mentioned above, Ebstein's disease can develop without any particular symptoms, but in Japan, with its aging population, cases such as the present case are rare but still possible. In the adult population with mostly

degenerative cardiac disease, the addition of Ebstein's disease with its many variations may make the treatment strategy more complex and difficult. This case suggests that even in asymptomatic Ebstein's disease, surgical intervention should be considered when other left ventricular procedures are necessary, depending on the severity of the disease.

3. Conclusion

Aortic valve replacement and cone surgery were performed simultaneously for Ebstein's disease, which was found incidentally during a thorough examination of patients with severe aortic regurgitation, with good results.

Disclosure statement

The authors declare no conflict of interest.

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Effectiveness of Sodium Creatine Phosphate Combined with Immunoglobulin in the Treatment of Patients with Viral Myocarditis

Fen Yang[1], Meijuan Ma[2]*

[1]Department of Respiratory and Critical Care Medicine, Shaanxi Provincial People's Hospital (Xixian), Xi'an 710068, Shaanxi Province, China
[2]Department of Cadre Physical Examination Center, Shaanxi Provincial People's Hospital , Xi'an 710068, Shaanxi Province, China

***Corresponding author:** Meijuan Ma, dymameijuan@163.com

Abstract: *Objective:* To study the effect of using sodium creatine phosphate combined with immunoglobulin therapy in the treatment of patients with viral myocarditis. *Methods:* Fifty-six cases of viral myocarditis patients were selected and randomly grouped, with 28 cases in each group. The study group underwent treatment using sodium creatine phosphate combined with immunoglobulin, while the control group underwent treatment using immunoglobulin. The outcome differences were compared. *Results:* After treatment, the study group showed significantly better cardiac function indexes, significantly lower myocardial enzyme spectrum indexes, significantly lower inflammatory mediator levels, and significantly shorter clinical symptom disappearance time as well as recovery time of myocardial enzyme spectrum as compared to the control group ($P < 0.05$). *Conclusion:* The effect of using sodium creatine phosphate combined with immunoglobulin in the process of treating patients with viral myocarditis is ideal.

Keywords: Creatine phosphate; Immunoglobulin; Viral myocarditis; Effects

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1. Introduction

Viral myocarditis is a type of cardiovascular disease in which the virus invasion leads to the patient's heart function being affected. The main clinical symptoms include fever, palpitations, respiratory tract infection, etc., and severe cases may even lead to sudden death. Currently, there is no effective method to treat the condition of patients with viral myocarditis [1], as its clinical treatment is difficult. The implementation of comprehensive treatment for patients is essential, with its main objective of inhibiting viral replication and strengthening the patient's body immunity. Clinical research showed that sodium creatine phosphate can stabilize the cell membrane and has antioxidant properties, but its single-use effect is unsatisfactory. Immunoglobulin was found to strengthen immune function, reduce viral differentiation, and improve the patient's myocardial injury. In

this paper, 56 patients were selected to study the effect of using sodium creatine phosphate combined with immunoglobulin in the treatment of patients with viral myocarditis.

2. Materials and methods

2.1. General information

Fifty-six patients with viral myocarditis were recruited between January and December 2023, which were then grouped into study and control groups with 28 cases each using drawing lots. There were 19 males and 9 females in the study group, with an age range of 6–14 years and a mean age of 9.22 ± 2.66 years, while there were 18 males and 10 females in the control group, with an age range of 5–15 years and a mean age of 9.21 ± 2.65 years. There was no significant difference in gender and age ($P > 0.05$).

2.2. Methods.

The control group received immunoglobulin treatment with a 50 mg intravenous drip once daily. The study group received sodium creatine phosphate combined with immunoglobulin treatment, with a 50 mg immunoglobulin intravenous drop once daily and 300 mg sodium creatine phosphate intramuscular injection once daily. Both groups received treatment for two weeks.

2.3. Observation indexes

The cardiac function indexes after treatment, cardiac enzyme spectrum indexes after treatment, inflammatory mediator levels after treatment, clinical symptoms disappearance time, and cardiac enzyme spectrum recovery time of the control and study groups were compared.

2.4. Statistical analysis

Statistical analysis was carried out using SPSS 25.0 software, data were expressed as [n (%)] and mean ± standard deviation (SD), with the implementation of χ^2 test and t-test. A P value of less than 0.05 indicated a statistically significant difference.

3. Results

Tables 1 to **4** show that after treatment, the study group had significantly better cardiac function indexes, significantly lower myocardial enzyme profile indexes, significantly lower inflammatory mediator levels, and significantly shorter clinical symptom disappearance time and recovery time of myocardial enzyme profile as compared to the control group ($P < 0.05$).

Table 1. Comparison of cardiac function indexes after treatment (mean ± SD)

Group	Ventricular ejection fraction (%)	Ratio of peak early mitral diastolic blood flow velocity to peak late mitral diastolic blood flow velocity	Ventricular short-axis shortening (%)
Study group (n = 28)	65.67 ± 5.74	0.50 ± 0.05	33.14 ± 5.22
Control group (n = 28)	57.76 ± 4.88	0.57 ± 0.08	26.74 ± 4.77
t value	5.5555	3.9263	4.7893
P value	< 0.05	< 0.05	< 0.05

Table 2. Comparison of myocardial enzyme profile indexes after treatment (mean ± SD; IU/L)

Group	Lactate dehydrogenase	Creatine kinase	Aspartate aminotransferase	Creatine kinase isoenzyme
Study group (n = 28)	57.48 ± 11.62	142.05 ± 19.52	29.48 ± 1.77	25.88 ± 4.36
Control group (n = 28)	76.51 ± 15.57	252.12 ± 27.47	34.01 ± 2.42	37.33 ± 6.37
t value	5.1831	17.2834	7.9949	7.8489
P value	< 0.05	< 0.05	< 0.05	< 0.05

Table 3. Comparison of inflammatory mediator levels after treatment (mean ± SD; ng/L)

Group	IL-6	IL-8	CRP	TNF-α
Study group (n = 28)	0.15 ± 0.07	1.04 ± 0.11	3.58 ± 1.02	13.84 ± 2.04
Control group (n = 28)	0.25 ± 0.12	1.38 ± 0.22	6.77 ± 1.85	20.35 ± 2.82
t value	3.8089	7.3144	7.9903	9.8973
P value	< 0.05	< 0.05	< 0.05	< 0.05

Table 4. Comparison of the time of disappearance of clinical symptoms and the time of recovery of cardiac enzyme spectrum (mean ± SD; d)

Group	Time to the disappearance of clinical symptoms	Recovery time of myocardial enzyme profile
Study group (n = 28)	11.06 ± 2.61	23.52 ± 2.78
Control group (n = 28)	18.02 ± 2.36	34.66 ± 3.71
t value	10.4664	12.7151
P value	< 0.05	< 0.05

4. Discussion

Patients with viral myocarditis have a more complex pathogenesis, in which a large number of inflammatory cytokines are released in the patient's body, causing continuous damage to cardiomyocytes and leading to cardiac dysfunction.

Clinical practice has confirmed the high feasibility of using sodium creatine phosphate combined with immunoglobulin therapy in the treatment of patients with viral myocarditis [2,3]. The implementation of the combination of drugs for patients provides myocardial nutrition to patients, significantly reduces the damage to patients' cardiomyocytes, avoids further apoptosis, increases the amount of blood transfusion to the patient's heart, and promotes the significant improvement of patient's symptoms [4-6], thereby significantly improving the effect of patient recovery. With various drug combinations, damaged cardiomyocytes were effectively repaired, and immune function was promoted significantly [7-10].

This study concluded that compared to the control group, the study group's cardiac function indexes were significantly better after treatment, the cardiac enzyme spectrum indexes were significantly lower after treatment, the inflammatory mediator level was significantly lower after treatment, and the time for clinical symptoms to disappear as well as the time for cardiac enzyme spectrum to recover was significantly shorter (P < 0.05). It was concluded that the inflammatory response was involved in the disease occurrence and development, and aggravation of the patient's condition would significantly increase the level of inflammatory mediators. Therefore, the monitoring of these data changes can be used in the assessment of clinical treatment effectiveness, as well as in the assessment of patient prognosis. After the implementation of the combination of drugs given to the patient, the patient's cardiac enzymes were reduced, and cardiac function was restored,

thus proving that the drug was safe to use. The use of the two drugs will synergize the effect of synergistic action, and significantly strengthen the clinical therapeutic effect on patients. The use of sodium creatine phosphate can provide a large amount of myocardial energy, promote the maintenance of normal physiological functions, protect the patient's cardiomyocytes, and effectively restore the patient's cardiac function. The use of immunoglobulin can remove the virus from the patient's body and promote the effective recovery of the patient.

In conclusion, the use of sodium creatine phosphate combined with immunoglobulin in the treatment of patients with viral myocarditis has an ideal effect, with significantly better cardiac function indexes, significantly lower myocardial enzyme indexes, significantly lower inflammatory mediator levels, significantly shorter clinical symptom disappearance time and myocardial enzyme recovery time, which is worth promoting in the clinic.

Disclosure statement

The authors declare no conflict of interest.

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Clinical Effects of Sildenafil in the Treatment of Congenital Heart Disease with Pulmonary Hypertension

Meijuan Ma[1], Fen Yang[2]*

[1]Department of Cadre Physical Examination Center, Shaanxi Provincial People's Hospital , Xi'an 710068, Shaanxi Province, China
[2]Department of Respiratory and Critical Care Medicine, Shaanxi Provincial People's Hospital (Xixian), Xi'an 710068, Shaanxi Province, China

***Corresponding author:** Fen Yang, 13227822115@126.com

Abstract: *Objective:* To analyze the improvement of mean pulmonary arterial pressure and oxygenation index as well as the therapeutic effect of sildenafil treatment in patients with congenital heart disease and pulmonary arterial hypertension. *Methods:* A total of 104 patients with congenital heart disease and pulmonary arterial hypertension were recruited from February 2023 to January 2024 and grouped into study and control groups using a randomized numerical table, with 52 patients in each group. The study group received sildenafil treatment, while the control group received conventional treatment. The therapeutic effects of both groups were analyzed and compared. *Results:* The study group had an average pulmonary arterial pressure of 26.23 ± 2.16 mmHg, an oxygenation index of 241.63 ± 4.86, and a total effective treatment rate of 98.08%, which was significantly better than the control group ($P < 0.05$). *Conclusion:* By implementing sildenafil treatment for patients with congenital heart disease and pulmonary hypertension, the mean pulmonary artery pressure and oxygenation index of the patients improved significantly, and the effective rate of treatment increased significantly.

Keywords: Congenital heart disease; Pulmonary hypertension; Sildenafil therapy

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1. Introduction

Pulmonary hypertension is A common complication of congenital heart disease which not only adversely affects the patient's recovery but also increases the mortality rate. At this stage, the main treatment for this complication is the use of appropriate medication, and patients can use sildenafil under the guidance of the doctor, which is safer and can significantly improve the patient's condition. This study was conducted on 104 patients with congenital heart disease and pulmonary hypertension treated between February 2023 and January 2024.

2. Materials and methods

2.1. General information

A total of 104 patients with congenital heart disease and pulmonary hypertension treated between February 2023 and January 2024 were recruited for this study, and their basic data are shown in **Table 1**.

Table 1. Basic data of patients with congenital heart disease and pulmonary hypertension

Group	Male patients	Female patients	Age	Average age
Study group (52 cases)	25 cases	27 cases	43–78years	57.9 ± 8.2 years
Control group (52 cases)	27 cases	25 cases	46–80 years	60.3 ± 7.6 years

There was no statistically significant difference between the general information of the above two groups ($P > 0.05$). Consent was obtained from the patients and their families for this study.

2.2. Methods

Conventional treatment was implemented for the patients in the study group, and calcium channel blockers, vasodilators, diuretics, anticoagulants, and cardiotonic agents were used for the patients at regular intervals [1,2]. The treatment lasted for 8 weeks, and the patients were closely observed for any adverse reactions during the treatment period.

In addition to the implementation of conventional treatment for patients in the experimental group, sildenafil treatment is implemented at the same time. Sildenafil was given thrice daily, with 20 mg each time, and the treatment lasted for 8 weeks. During the treatment period, patients were closely monitored for any adverse reactions.

2.3. Observation indexes

The average pulmonary artery pressure and oxygenation index of patients with congenital heart disease and pulmonary hypertension before and after treatment were compared between the two groups. The treatment effect of the patients was observed, where “very effective” is indicated by significantly improved heart function, “effective” is indicated by improved heart function, and “ineffective” is indicated by no improvement in heart function or further deterioration. The total effective rate is the sum of “very effective” and “effective” among all cases × 100%.

2.4. Statistical analysis

SPSS 22.0 statistical software was applied, a *t*-test was used for the measurement data and expressed as mean ± standard deviation (SD), while χ^2 test was used for the count data and expressed as [*n* (%)]. A *P* value of less than 0.05 indicated a statistically significant difference.

3. Results

3.1. Comparison of the average pulmonary artery pressure and oxygenation index of the two groups before and after treatment

Before treatment, there were no significant differences in the mean pulmonary artery pressure and oxygenation index of both groups. However, the study group showed significantly better mean pulmonary artery pressure and oxygenation index as compared to the control group ($P = 0.00$), as shown in **Table 2**.

Table 2. Comparison of mean pulmonary artery pressure and oxygenation index before and after treatment (mean ± SD)

Group	Before treatment		After treatment	
	Mean pulmonary artery pressure (mmHg)	Oxygenation index	Mean pulmonary artery pressure (mmHg)	Oxygenation index
Study group (52 cases)	59.13 ± 11.12	192.12 ± 5.04	26.23 ± 2.16	241.63 ± 4.86
Control group (52 cases)	58.24 ± 11.47	191.68 ± 5.43	39.42 ± 2.57	198.14 ± 5.27
t	0.402	0.428	28.332	43.746
P	0.689	0.669	0.000	0.000

3.2. Comparison of the therapeutic effect of the two groups

Table 3 shows that the total effective treatment rate of the study group was 98.08%, which was significantly higher than the control group of 86.54% ($P = 0.027$).

Table 3. Comparison of the therapeutic effect [*n* (%)]

Group	Very effective	Effective	Ineffective	Overall effective rate
Study group (52 cases)	30 (57.69)	21 (40.38)	1 (1.92)	51 (98.08)
Control group (52 cases)	15 (28.85)	30 (57.69)	7 (13.46)	45 (86.54)
χ^2				4.875
P				0.027

4. Discussion

In recent years, the phenomenon of late marriage and childbearing has become increasingly serious, coupled with the implementation of the two-child policy in China, the number of women of advanced maternal age has increased, which has led to a higher rate of children with congenital heart disease [3-5]. In children with congenital heart disease, due to the body being in a long-term left-to-right shunt state and increased pulmonary vascular resistance, it is easy to induce pulmonary hypertension as a complication. The emergence of this complication will pose a further threat to the physical health of the child [4,6].

Sildenafil has been increasingly used in the treatment of congenital heart disease and pulmonary arterial hypertension in recent years. This drug was mainly used to treat male erectile dysfunction previously, but lately, it was found to have a better therapeutic effect on pulmonary arterial hypertension with fast effect, simple usage, can effectively dilate the blood vessels, reduce the pulmonary vascular resistance, increase the concentration of oxygen in the blood, thereby achieving the therapeutic effect of improving pulmonary hypertension [7-9].

In this study, 52 patients in the study group were treated with sildenafil, and the average pulmonary artery pressure was 26.23 ± 2.16 mmHg, the oxygenation index was 241.63 ± 4.86, which was significantly better than the control group's average pulmonary artery pressure (39.42 ± 2.57 mmHg) and oxygenation index (198.14 ± 5.27). Moreover, the total effective treatment rate of the study group reached 98.08%, which was significantly higher than that of the control group (86.54%). This shows that with the implementation of sildenafil treatment for patients with congenital heart disease and pulmonary hypertension, the average pulmonary artery pressure and oxygenation index of patients significantly improved, and the treatment efficiency was high.

In conclusion, patients with congenital heart disease, after the complication of pulmonary hypertension, can follow the doctor's instructions, through the treatment of sildenafil to relieve the disease, the drug has a

better therapeutic effect on congenital heart disease and pulmonary arterial hypertension and has a high degree of safety.

Disclosure statement

The authors declare no conflict of interest.

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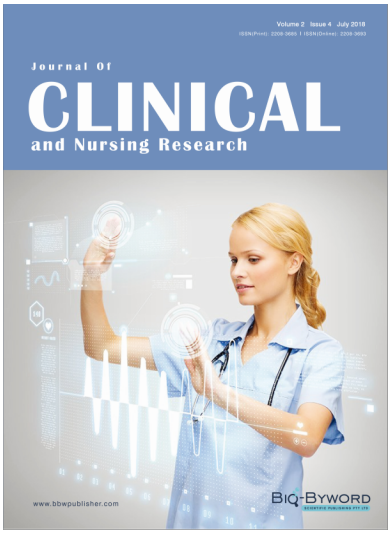

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