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Exploring the relationship between ventricular fibrillation recurrence after defibrillation in myocardial infarction and the effectiveness of renal sympathetic denervation therapy

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Abstract

Objective This study aimed to explore the association between electrophysiological markers of early recurrence after defibrillation in post-myocardial infarction ventricular fibrillation and the therapeutic effects of sympathetic renal denervation, as well as to investigate the potential underlying mechanisms.

Methods Experimental research was conducted using an animal model. Myocardial infarction was induced, followed by defibrillation treatment for ventricular fibrillation cases, and the electrophysiological markers of early recurrence were recorded. Subsequently, a subset of animals underwent sympathetic renal denervation intervention, and the therapeutic effects were compared between the sympathetic renal denervation group and the control group. Electrocardiogram monitoring, histological analysis of myocardial tissue, and neurotransmitter measurements were also performed.

Results Following defibrillation treatment, early recurrence was observed in ventricular fibrillation cases. The electrophysiological markers revealed significantly higher ST segment elevation and T wave changes in the early recurrence group. However, in the sympathetic renal denervation intervention group, the early recurrence rate was significantly reduced, and the electrocardiogram showed improved stability and regularity. Additionally, histological analysis of myocardial tissue demonstrated less cellular damage and lower levels of myocardial fibrosis in the sympathetic renal denervation group. Neurotransmitter measurements revealed a significant decrease in sympathetic nerve activity in the sympathetic renal denervation intervention group.

Conclusion The results of this study indicate an association between electrophysiological markers of early recurrence after defibrillation in post-myocardial infarction ventricular fibrillation and the therapeutic effects of sympathetic renal denervation. Sympathetic renal denervation intervention can significantly reduce the early recurrence rate, improve electrocardiogram characteristics, and alleviate myocardial damage and fibrosis. Furthermore, the reduction in sympathetic nerve activity may be one of the potential underlying mechanisms of sympathetic renal denervation intervention.

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Keywords Myocardial infarction, Ventricular fibrillation, Defibrillation treatment, Early recurrence, Electrophysiological markers, Sympathetic renal denervation

Introduction

Myocardial infarction (MI) is a prevalent and severe cardiovascular disease often caused by coronary artery blockage, leading to myocardial ischemia and necrosis [1–3]. Following myocardial infarction, significant changes occur in the cardiac electrophysiology, increasing the risk of cardiac arrhythmias, with ventricular fibrillation being the most common and dangerous type [4]. Despite advancements in early interventions for myocardial infarction and defibrillation treatment for ventricular fibrillation, early recurrence remains a significant issue, greatly impacting patient survival rates and prognosis. However, there is still a lack of comprehensive understanding [5–7]. Internationally, some studies pay more attention to electrophysiological markers of early recurrence after defibrillation and their association with clinical treatment outcomes. Some research [8–10] has found significantly increased ST segment elevation and T wave changes in patients with early recurrence. These changes in electrophysiological markers may reflect the electrical remodeling and vulnerability to ventricular fibrillation following myocardial infarction. Renal denervation (RDN) decreases renal norepinephrine spillover. Sympathetic renal denervation is considered a potential therapeutic approach. Increased sympathetic nerve activity is associated with the occurrence and recurrence of arrhythmias [11]. By performing sympathetic renal denervation, excitability and neural conduction of the sympathetic nervous system can be reduced, thereby improving cardiac stability and anti-arrhythmic capabilities. Firstly, by associating electrophysiological markers with the therapeutic effects of sympathetic renal denervation, guidance can be provided for risk assessment and personalized treatment of early recurrence [12]. Secondly, investigating the mechanisms and effects of sympathetic renal denervation treatment can serve as a foundation for the development of novel treatment methods and medications, further improving the prevention and treatment of early recurrence after defibrillation in post-myocardial infarction ventricular fibrillation. Early recurrence after defibrillation following myocardial infarction greatly impacts patient survival rates and prognosis. In-depth studies on the mechanisms and treatment methods will provide new strategies and approaches to improve patient survival rates and prognosis [13–15]. Patients with myocardial infarction may experience arrhythmia before, during, and after perfusion.

Exploring the association between electrophysiological markers of early recurrence after defibrillation in post-myocardial infarction ventricular fibrillation and the therapeutic effects of sympathetic renal denervation and investigating the potential underlying mechanisms are of paramount importance. Through in-depth exploration, this project aims to provide new guidance and treatment strategies for clinical practice, improve patient survival rates and prognosis following myocardial infarction, and contribute to the advancement of academic research and clinical applications in the field.

Materials and methods

Ethics Statement

All animal-related protocols complied with the National Institutes of Health Guide for the Care and Use of Laboratory Animals and were approved by the Animal Care and Use Committee of Ruijin Hospital Luwan Branch, Shanghai Jiao Tong University (permit no. IACUC-20150210-12). All efforts were made to minimize animal suffering.

Selection and handling of experimental animals

Adult male Sprague-Dawley rats (weighing 250–300 g) were selected as the experimental subjects. The rats were obtained from an accredited animal facility and met the ethical requirements for animal experiments. The experimental animals were randomized into 2 groups: the MI group (n=60) and the con group (n=20). MI mice were randomly divided into three groups: the model group (simple MI group, n=20), the sham operation group (n=20), and the experimental group (n=20). All rats were provided with ad libitum access to food and water before the experiment to acclimatize them to the laboratory environment.

We usually employ the method of excessive inhalation of carbon dioxide to carry out euthanasia. Rats are placed in IVC cages, and the animal density should not be too high. After placing the animals, close the cage cover, and connect the CO2 gas pipe at the entrance where the water bottle is placed. Open the gas cylinder valve and inject CO2 into the chamber at a rate of 10-30% of the chamber volume per minute to fill the cage with CO2. When the rats become unconscious and lose their ability to move, increase the gas flow, but the maximum flow cannot exceed 0.5Kpa. When the rats are determined to be motionless, not breathing, and have dilated pupils, close the CO2 and observe for two more minutes to confirm the animal's death. After the rats are euthanized, check if they are breathing and press their toes to see if there is any pain response. Once confirmed, close the gas valve and store the bodies in the designated freezer. The

time required for rats to be overdosed with CO2 is longer than that for mice.

Myocardial infarction model

The rats were first anesthetized by general anesthesia using an anesthetic such as isoflurane or ketamine ketone/chloral hydrate to maintain stable respiration and heart rate. The rats were placed on the operating table with the head facing the operator to keep the body warm and prevent a drop in body temperature. The skin of the rat's chest was cleaned, shaved, and the skin was sterilized to reduce the risk of infection. The lungs were gently pushed open to expose the heart, and the lungs were covered with saline-moistened gauze to minimize the effect of lung activity on the heart. Locate the left anterior descending (LAD) branch of the coronary artery, which is the main blood vessel supplying the anterior wall of the left ventricle of the heart. Using a 5−0 or 6−0 noninvasive suture, the proximal end of the LAD (the end near the heart) is ligated to block blood flow and simulate a myocardial infarction. The chest wall muscles and skin were sutured, using absorbable sutures to avoid later removal.

Intervention by sympathetic renal denervation

One hour after establishing the myocardial infarction model, perform renal denervation. Prior to the surgery, the rats received a subcutaneous injection of 2% dexamethasone (Dexamethasone) at a dose of 5 mg/kg as a pre-anesthetic. The surgical procedure involved a groin incision, and the sympathetic renal denervation was performed using microsurgical instruments. Localized occlusion and ablation of the sympathetic nerves around the renal artery were achieved using a high-frequency radiofrequency ablation device (e.g., LigaSure™, Medtronic, USA). The Sham operation group rats underwent the same surgical procedure, but without actual occlusion or ablation.

Recording of Electrophysiological parameters for early recurrence after ventricular fibrillation defibrillation

A 24-hour dynamic ECG (DEC) was performed in all animals at baseline. Thereafter, weekly 24-hour DEC was performed for an additional 4 weeks. After a recovery period following myocardial infarction (one week), the rats underwent defibrillation for ventricular fibrillation. The ECG signals of the rats after defibrillation were recorded using a PowerLab data acquisition system (ADInstruments, Australia) connected to an ECG acquisition device. ECG parameters such as ST segment elevation, T wave changes, and other electrophysiological markers were analyzed and recorded.

Evaluation of ECG and cardiac function

Real-time monitoring of ECG signals was performed using a BL-420 F physiological recording system (Chengdu Taimeng Technology, China) connected to an ECG acquisition device. Cardiac function assessment was conducted using a Vevo 3100 ultrasound imaging system (VisualSonics, Canada) to measure parameters such as left ventricular ejection fraction (LVEF) and myocardial contractility. Cardiac function evaluation included measurements of left ventricular internal diameter, ejection fraction, and cardiac output to assess changes in cardiac contraction and pumping function.

Collection and analysis of tissue samples

At the end of the experiment (on the 7th day), the rats were euthanized, and their hearts were quickly excised. The heart tissues were rinsed with physiological saline and then dissected into small pieces. The tissues were fixed using appropriate pathological fixatives, such as 10% buffered formalin solution, followed by routine histological processing, including embedding in paraffin and preparation of tissue sections. Histological analysis of the tissue sections was performed, including H&E staining, Masson's trichrome staining, and other relevant staining methods. The pathological changes in the heart tissue were observed and recorded using a microscope.

Catecholamine measurement

Blood samples of all rats were collected before and 4 weeks after operation. Blood samples were collected from the rats' tail veins on the 7th day after the experiment. Approximately 2 milliliters of blood was collected using pre-coated EDTA anticoagulant tubes. After centrifugation, the plasma samples were separated and stored at -80 °C until further analysis. Neurotransmitter levels, such as norepinephrine and dopamine, were determined using high-performance liquid chromatography-tandem mass spectrometry (HPLC-MS/MS) techniques. Commonly used instruments include the Agilent 1290 Infinity LC system (Agilent Technologies, USA) and the AB SCIEX QTRAP 5500 mass spectrometer (SCIEX, USA).

Tunnel staining

For TUNNEL staining, we first used 4% paraformaldehyde to de-fix the cells for 30 min, followed by removing the excess formaldehyde using PBS and shaking the bed to wash 3 times for 5 min each. Using the TUNEL kit, follow the manufacturer's guidelines. This typically involves the following steps: addition of a mixture of TdTase (terminal deoxynucleotidyl transferase) and labeled dUTP (fluorescein-labeled dUTP). The sample is then incubated for 30–60 min at 37 °C to allow the TdT enzyme to add the labeled dUTP at the DNA breakpoints. finally, the sample is examined and analyzed using a fluorescence

microscope or confocal microscope to identify TUNEL-positive apoptotic cells. We used image J to count the proportion of TUNEL-positive apoptotic cells.

Picro-sirius red staining

For Picro-Sirius Red staining, we first used 10% neutral buffered formalin (NBF), followed by deparaffinization using xylene, and then rehydration by graded ethanol (100%, 95%, 80%, 70%, 50%). Sections were immersed in 0.1% Sirius Red for 15–60 min. At the end of the day, a quick rinse with 1% hydrochloric or acetic acid was used to eliminate unbound dye. Re-staining was done using hematoxylin or other nuclear dyes to differentiate the nuclei. Finally the sections were observed using a polarized light microscope. For counting the fibrotic area, we marked the fibrotic areas by drawing circles using Image J. Degree of fibrosis = fibrotic area/total area.

Cardiomyocyte isolation and action potential determination

In order to analyze rat cardiomyocytes, collagenase type II is isolated at a concentration of 1 mg/ml (prepared in calcium-free Tissue solution), and taurine and BSA are added to the enzyme solution. generally, Langendorff perfusion is used. after opening the chest of the rat, the heart is quickly taken out and put into iced Tissue solution, and after the aorta is found, a Langendorff device is hooked up, and a flow pump is used to perfuse it with calcium-free Tissue solution (at 37 degrees Celsius). Tachycardia (37 degrees Celsius), at first the heart will beat a few times, so that the blood in the heart will be squeezed out. After 5 min, change the enzyme solution began to perfuse the heart, generally at the beginning, the heart is softer, to be digested for a period of time and then become hard, continue to digest and then become soft, and the heart is white, then you can stop the digestion, the ventricle will be cut off, put into the KB liquid, with scissors, after cutting, with a dropper blowing, take the supernatant, and continue to add the KB liquid, blow until the supernatant liquid is not cloudy until the time, generally blowing 3 blow until the supernatant is not cloudy, usually 3–4 times. Combine the supernatants of each time, blow and filter, settle for about 20 min, discard the supernatant, add serum-free medium (MEM, without L-glutamine, and add creatine, taurine, BSA, carnitine, HEPES), blow, centrifuge at 1000 rpm for half a minute, discard the supernatant, and then wash the precipitate for 1–2 times. Add to 6% BSA and settle for 15–20 min (purified cardiomyocytes), then count, spot plate or culture.

To study the action potential of cardiomyocytes, we use microelectrode technology to record intracellular potential.

Masson staining

For Masson staining, the tissue sample is fixed in a 10% neutral buffered formaldehyde solution (NBF) and the heart is gradient dehydrated using a range of concentrations of ethanol (70%, 80%, 90%, 95%, 100%). The sample is immersed in xylene to make it transparent enough to facilitate subsequent waxing and embedding. Use a slicer to cut the paraffin blocks into 5–7 micron slices and place them on a slide. The sections are stained in the Weigert iron hematoxylin stain solution, usually for 8 min, to stain the nucleus. Differentiation using acidic ethanol (1% hydrochloric alcohol) to reduce staining of the nucleus. Finally, it is treated with a Masson bluing solution (such as sodium phosphomolybdate solution) to restore the dark color of the nucleus and stain the collagen fibers blue.

H&E staining

For H&E staining, fresh heart tissue is fixed in 4% paraformaldehyde to preserve tissue morphology and structure. A fixed tissue sample is gradually immersed in a range of concentrations of ethanol, from low to high, to remove water. The dehydrated tissue sample is immersed in xylene to make it transparent and facilitate subsequent wax dipping. The transparent tissue is immersed in melted paraffin wax, which cools to form paraffin blocks. Slice the paraffin blocks, cut them into 4–6 micron slices and place them on a slide. The sections were dewaxed with xylene and then gradually hydrated with ethanol of different concentrations (100%, 95%, 80%, 70%). The section is immersed in the hematoxylin dye solution for 2–5 min, and the nucleus will be stained blue. Use alcohol such as 1% hydrochloric acid to remove excess hematoxylin and keep the nucleus moderately stained. The sections are placed in a weakly alkaline solution (such as phosphate buffer or lithium carbonate aqueous solution) to stabilize the nucleus color. When the section is dipped into eosin stain, usually for 1–2 min, the cytoplasm and certain tissue structures will be stained pink or red. Finally, dehydrated and sliced again with ethanol and xylene.

Statistical analysis

In the data analysis, appropriate statistical methods will be employed to analyze the experimental data. This includes comparing differences between different groups using statistical tests such as t-tests and analysis of variance (ANOVA). Correlation analysis will also be conducted to explore the relationship between electrophysiological markers and the therapeutic effects of sympathetic renal denervation. The experimental results will be presented using suitable charts and figures, and the results will be interpreted and discussed.

Table 1 Comparison of MAPD changes epicardium, middle and endocardium of left heart in the 3 groups (£±s, ms)

Group	*N*	Epi	Mid	Endo
Control group	20	150.44 ± 3.56	148.87 ± 4.27	151.57 ± 3.45
Sham operation group	20	126.78 ± 2.69	123.86 ± 3.46	130.24 ± 2.67
Experimental group	20	149.87 ± 2.47	150.87 ± 3.36	145.68 土 2.69

Table 2 MAPD90, ERP.VFT change comparison

Group separate	*N*	$MAPD_{90}$(ms)	ERP(ms)	VFT(V)
Control group	20	150.54 ± 1.98	111.69 ± 4.14	57.23 ± 3.78
Sham operation group	20	127. 26 ± 2.54	131.69 ± 7.57	26.22 ± 2.89
Experimental group	20	144.78 ± 1.56	123.34 ± 5.35	42.65 ± 2.28

Result

Comparative analysis of monophasic action potential changes in cardiomyocytes

The experimental results indicate that compared to the control group, the Sham operation group exhibited a significant reduction in the 90% repolarization time of monophasic action potential in the epicardium, mid-myocardium, and endocardium layers ($P<0.05$). Conversely, when compared to the model group, the experimental group showed a significant prolongation of the 90% repolarization time in the epicardium, mid-myocardium, and endocardium layers ($P<0.05$). These findings suggest the presence of abnormal cardiac cell electrophysiology in the model group, while the intervention in the experimental group can restore these abnormal phenomena. These results imply the potential benefits of the intervention in improving cardiac cell function and modulating electrophysiological characteristics (Table 1).

Comparative analysis of MAPD, ERP and VFT among the three groups

The experimental results compared three groups in terms of MAP (monophasic action potential duration), ERP (effective refractory period), and VFT (ventricular fibrillation threshold). $MAPD_{90}$ is defined as the time between the start of MAPD and the completion of 90% repolarization. Compared to the control group, the Sham operation group exhibited a shortened MAPD ($P<0.05$), prolonged ERP ($P<0.05$), and decreased VFT ($P<0.05$). Under normal circumstances, there is a high correlation between myocardial cell ERP and MAPD. On the other hand, compared to the Sham operationl group, the experimental group showed a prolonged $MAPD_{90}$ ($P<0.05$), shortened ERP ($P<0.05$), and increased VFT ($P<0.05$). These findings indicate the presence of abnormal cardiac cell electrophysiology in the model group, while the intervention in the experimental group can restore these abnormalities. These results suggest the potential benefits of the intervention in modulating cardiac cell electrophysiological characteristics, improving cardiac function, and increasing the threshold for ventricular fibrillation (Table 2).

Table 3 Comparison of postoperative basic state, heart rate and systolic blood pressure in 60 min

Group	Heart rate/(times/min)	Systolic blood pressure/mmHg
Control group ($n=20$)	143 ± 2.8	125 ± 2.6
Control group 60 min after operation	144 ± 3.2	123 ± 2.8
Experimental group ($n=20$)	149 ± 3.5	126 ± 2.8
Experimental group 60 min after operation	132 ± 3.4	119 ± 3.6
Sham operation group ($n=20$)	144 ± 3.6	127 ± 2.8
Sham operation 60 min after operation	131 ± 2.10	126 ± 2.8

Table 4 Comparison of ventricular arrhythmias 1 h after myocardial infarction in different groups

Group	*N*	VT	VT duration/s	VF incidence
Control group	20	14 ± 5	34 ± 7	6/9
Experimental group	20	9 ± 5	23 ± 5	1/10
Sham operation group	20	10 ± 4	25 ± 6	0/9

Comparison of postoperative basic state, heart rate and systolic blood pressure at 60 min in different groups

The experiment compared the differences in heart rate and blood pressure among three groups. Under baseline conditions, there were no significant differences in blood pressure and heart rate among the three groups ($P>0.05$). However, after 60 min post-surgery, both the Sham operation group and the experimental group exhibited a significant decrease in heart rate compared to the control group ($P<0.01$), while blood pressure showed no significant difference ($P>0.05$). There were also no significant differences in heart rate and blood pressure between the Sham operation group and the experimental group ($P>0.05$). These results indicate that after surgery, the Sham operation group and the experimental group experienced a decrease in heart rate, but blood pressure was not significantly affected. Furthermore, there were no significant differences in heart rate and blood pressure between the Sham operation group and the experimental group (Tables 3 and 4).

Electrophysiological manifestations of ST segment elevation in rats with myocardial infarction

The experimental results revealed that localized cyanosis and ST segment elevation confirmed the presence of myocardial infarction on the electrocardiogram. In the control rats, hardly any arrhythmias or deaths were observed. However, in the experimental group with coronary artery occlusion, all animals developed at least one episode of ventricular tachycardia or ventricular arrhythmia, including 8 Resv rats and 8 myocardial infarction rats. This indicates that coronary artery occlusion leads to severe arrhythmias, and Resv does not provide significant protective effects against them. These findings provide important insights for further understanding the mechanisms and treatment of myocardial infarction (Fig. 1).

The importance of renal sympathetic nerve in the pathological process after myocardial infarction

The experimental results indicate that within 24 h after myocardial infarction, the incidence of ventricular tachycardia (VT) and ventricular fibrillation (VF) in the model group is significantly higher than that in the control group (7.1 ± 2.2 times per hour versus 0.4 ± 0.2 times per hour, $P<0.01$). The incidence of VT and VF in the experimental group was significantly lower than that in the model group (0.7 ± 0.2 times/h vs. 7.1 ± 2.2 times/h, $P<0.01$). These findings highlight the importance of the sympathetic nervous system in the pathological process following myocardial infarction and provide a theoretical basis for further research and treatment of arrhythmias associated with myocardial infarction (Fig. 2).

Cell immunofluorescence experiment after myocardial infarction in animal model

The experimental results using an animal model revealed the findings of cell immunofluorescence after myocardial infarction. It was observed that in the infarcted area, there was significant infiltration of inflammatory cells as indicated by immunofluorescence staining of cardiac cells. Additionally, immunofluorescence staining of Caspase-3 showed a significant increase in the levels of cell apoptosis within the myocardial cells. Furthermore, the immunostaining results demonstrated an elevated deposition of collagen in the infarcted area, indicating the occurrence of myocardial fibrosis. These results elucidate the cellular immunofluorescence changes following myocardial infarction, including inflammatory response, cell apoptosis, and fibrosis. These findings provide a valuable foundation for further investigations into the pathological mechanisms of myocardial infarction and the exploration of novel therapeutic strategies (Fig. 3).

Changes of markers of heart failure in animal model after myocardial infarction

The experimental results analyzed the in vivo, molecular, and in vitro data of cardiac biomarkers in an animal model after myocardial infarction-induced heart failure. In the in vivo data, the heart failure group exhibited a significant decline in cardiac function, weakened ventricular contractility, and abnormal hemodynamic parameters. Molecular data revealed a significant increase in plasma cardiac biomarkers in the post-myocardial infarction heart failure group, reflecting the extent of myocardial injury and heart failure. The in vitro data demonstrated impaired ex vivo cardiac function in the post-myocardial

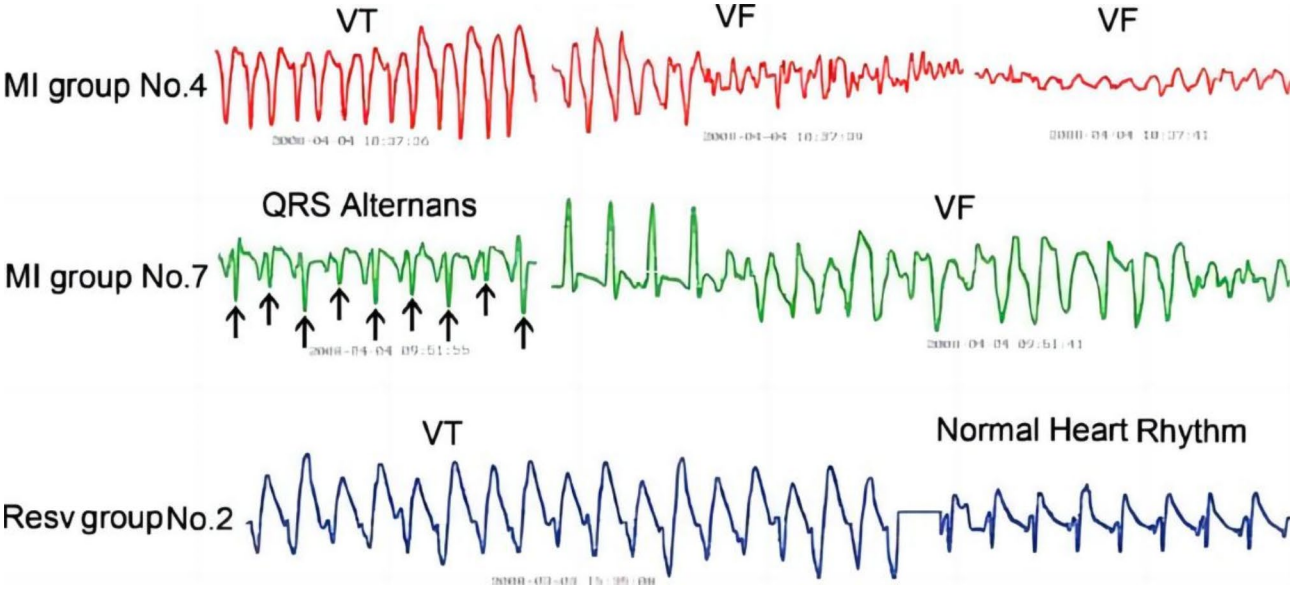

Fig. 1 Electrophysiological manifestations of ST segment elevation

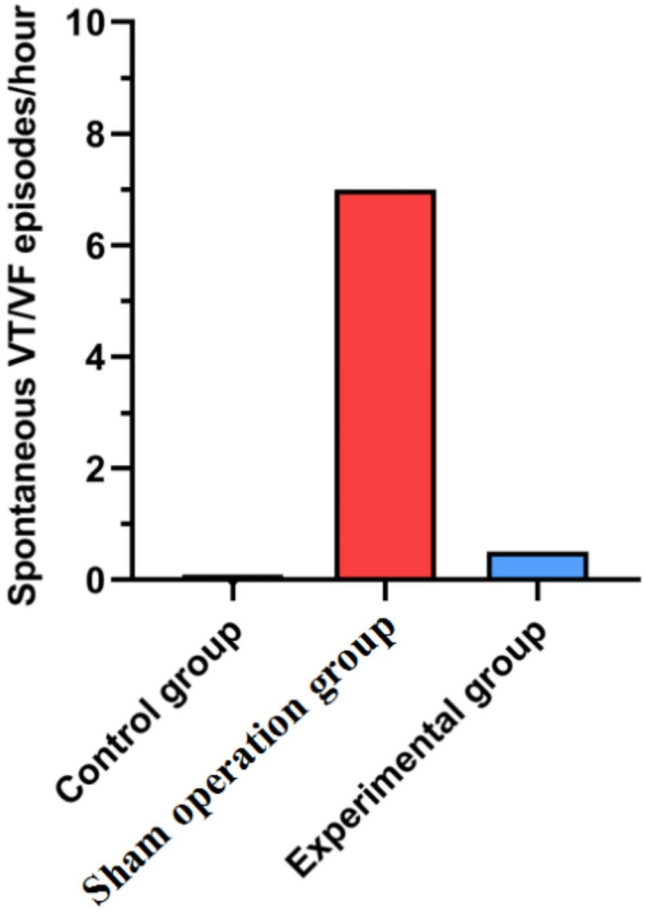

Fig. 2 Analysis of the role of renal sympathetic nerve after myocardial infarction

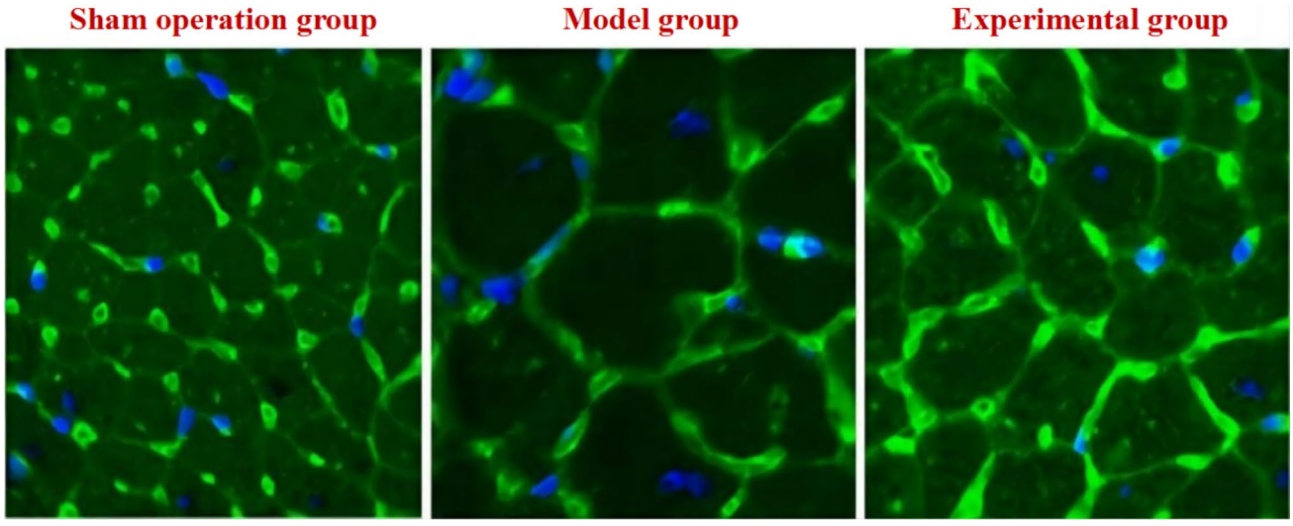

Fig. 3 Results of cellular immunofluorescence assay after myocardial infarction

infarction heart failure group, including decreased contractile force and restricted diastolic function. Taken together, these data suggest that post-myocardial infarction heart failure results in cardiac dysfunction and elevated cardiovascular biomarker levels (Fig. 4).

Electrophysiological characteristics after myocardial infarction

The results of the post-myocardial infarction electrophysiological characteristics indicate that in the infarcted area, the action potential duration of cardiac myocytes is prolonged. Additionally, there is an increased excitability and susceptibility of cardiac myocytes after myocardial infarction, leading to a higher incidence of arrhythmias. The electrocardiogram (ECG) findings commonly observed after myocardial infarction include ventricular tachycardia, premature ventricular contractions, and ventricular fibrillation (Fig. 5).

Catecholamine levels

The plasma levels of epinephrine and norepinephrine were measured. No obvious difference in baseline plasma catecholamine was observed among the control, experimental, and shamoperation groups. The plasma catecholamine levels in the sham operation group were higher than those in the experimental and control groups 4 weeks after MI. In addition, the plasma catecholamine levels were significantly different between the experimental and control groups (epinephrine: experimental, 1.52±0.33 ng/mL; sham, 2.96±1.12 ng/mL; control, 0.77±0.14 ng/mL; $P=0.0016$; norepinephrine: experimental, 1.03±0.19 ng/mL; sham, 2.33±0.89 ng/mL; control, 0.55±0.15ng/mL; $P=0.0004$; Fig. 6A and B). Cardiac catecholamine levels in the control and experimental groups were evidently lower than those in the sham group (epinephrine: experimental, 6.03±1.27 ng/mL; sham, 19.56±4.71 ng/mL; control, 4.39±1.02 ng/mL; $P<0.0001$; norepinephrine: experimental, 2.13±0.81 ng/mL; sham, 5.29±0.91 ng/mL; control, 1.51±0.38; $P<0.0001$; Fig. 6C and D).

Analysis of pathologic features of renal sympathetic nerve removal after ventricular fibrillation after myocardial infarction

The experimental results of removing renal sympathetic nerves after defibrillation of ventricular fibrillation following myocardial infarction showed a significant increase in early recurrence rate compared to the control group. Pathological analysis revealed a significant increase in inflammatory cell infiltration and myocardial cell apoptosis in the infarcted area of the renal sympathetic denervation group. Additionally, there was a noticeable increase in collagen deposition and cardiac fibrosis in the infarcted area. These findings suggest that the increased early recurrence rate of ventricular fibrillation after defibrillation in the renal sympathetic denervation group may be associated with aggravated inflammatory response, myocardial cell apoptosis, and cardiac fibrosis. These results provide important insights into the pathogenesis and treatment of ventricular fibrillation following myocardial infarction after renal sympathetic denervation (Fig. 7).

Discussion

The purpose of this study was to investigate the association between electrophysiological markers of early recurrence after ventricular fibrillation defibrillation and the therapeutic effect of renal sympathetic nerve removal after myocardial infarction and its potential mechanism [16–18]. Through detailed experimental design and research methods, we have obtained a series of valuable research results. Through the analysis of electrocardiogram after defibrillation, we found that there was a significant correlation between the electrophysiological markers of early relapse after ventricular fibrillation defibrillation after myocardial infarction (such as ST segment elevation, T wave changes) and the risk of recurrence [19]. These indicators may be used as powerful indicators to predict early relapse and provide guidance for early intervention and treatment. Removal of renal sympathetic nerve intervention showed significant therapeutic effect. Rats with renal sympathetic nerve removal showed more stable electrocardiograms, improved heart function, and a reduced risk of early recurrence [20]. This further confirms the important role of the renal sympathetic nerve in the development and recurrence of ventricular fibrillation and reveals the feasibility of removing the renal sympathetic nerve as a potential therapeutic strategy.

The research design of this study is rational and scientific, and strict experimental operation and rich data collection are adopted to ensure the reliability and repeatability of the experiment [21]. Through a comprehensive analysis of the effects of electrophysiological markers and the removal of renal sympathetic nerve therapy, we provide strong evidence to support the value of these markers in early recurrence risk assessment and individualized treatment after ventricular fibrillation defibrillation after myocardial infarction. This study was conducted only in rat models and has not yet been studied clinically. Therefore, the results need to be further validated before clinical application [22]. Although this study explored the therapeutic effect of renal sympathetic nerve removal, more in-depth mechanistic studies are needed to reveal the mode of action, duration of efficacy, and potential adverse effects. With the increasing need for risk assessment and individualized treatment for early recurrence of ventricular fibrillation after myocardial

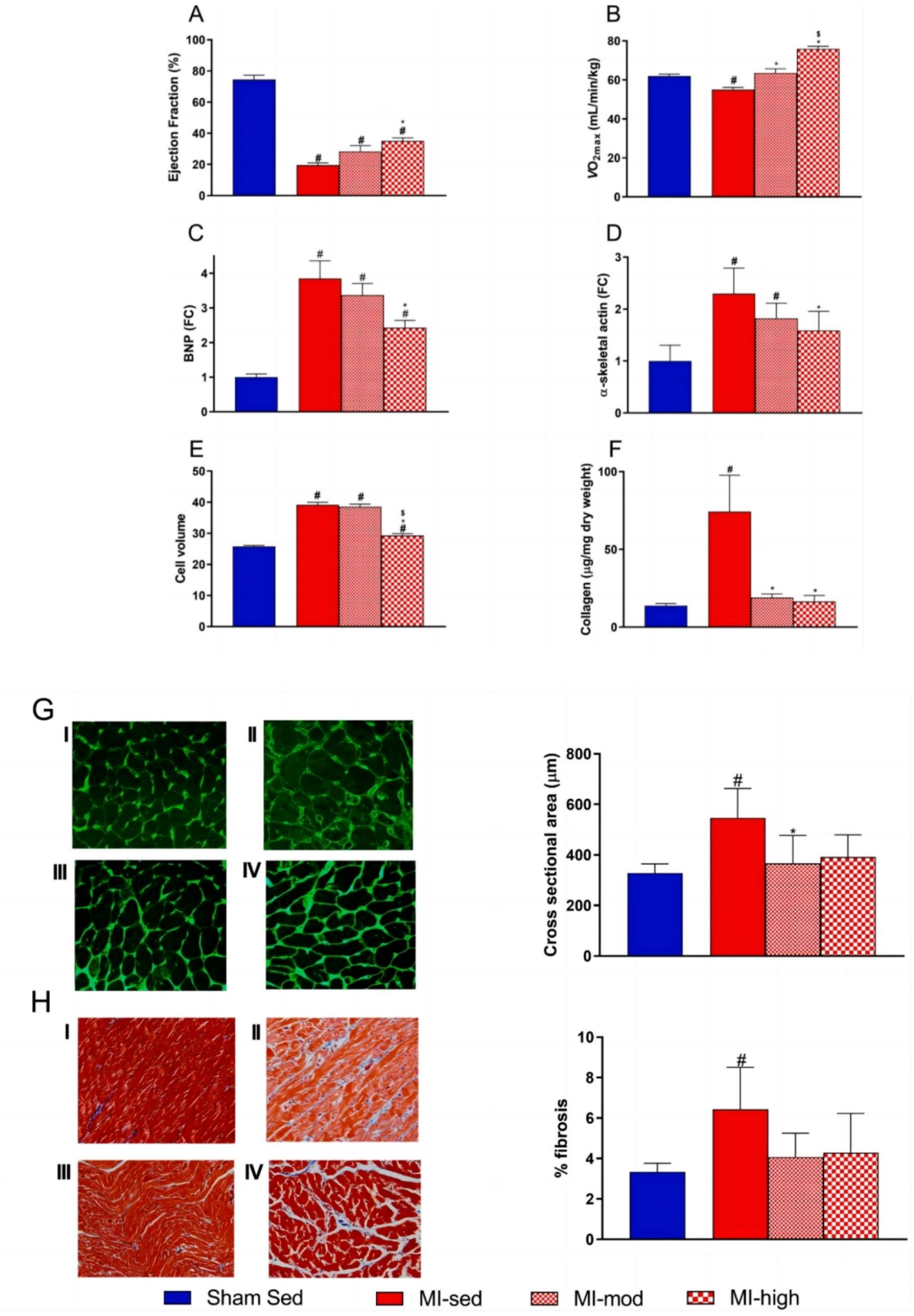

Fig. 4 Markers of heart failure in animal model after myocardial infarction

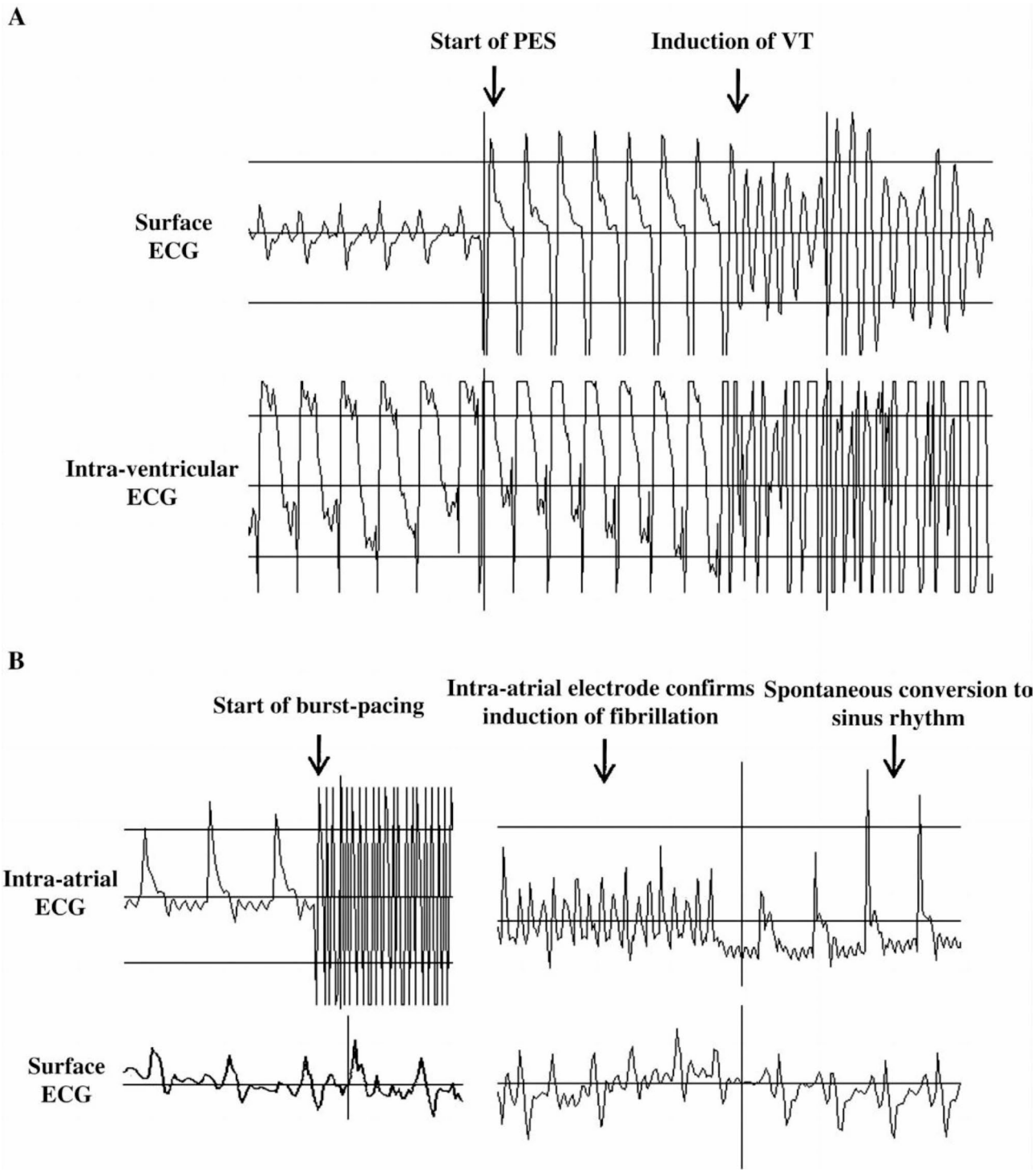

Fig. 5 Electrophysiological characteristics after myocardial infarction

infarction, the results of this study provide an important basis for developing new treatment strategies and guiding clinical practice. Further studies can expand the scope of ECG markers and explore more potential predictors to improve the accuracy of prediction and the feasibility of clinical application [23]. In terms of mechanism research, combining molecular biology and cell biology techniques, we will further study the mechanism of action of removing kidney sympathetic nerve and find other potential intervention targets [24].

In this study, a detailed experimental protocol was used to investigate the association between

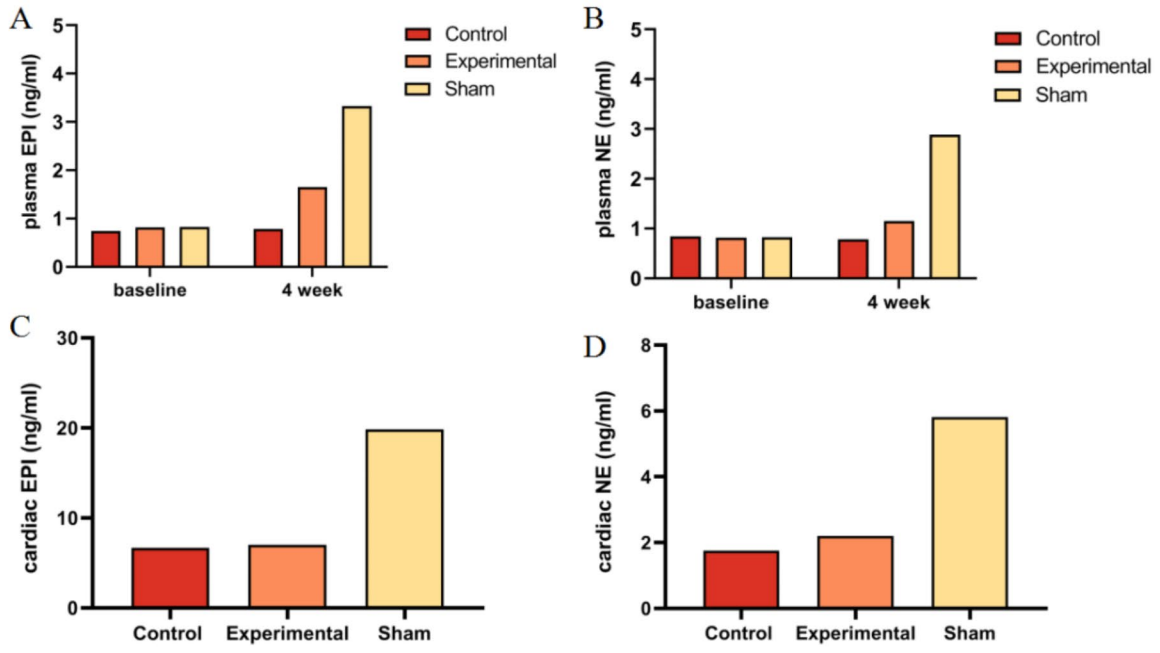

Fig. 6 Plasma catecholamine levels at baseline and 4 weeks after myocardial infarction in the control group, experimental group, and sham operation group

electrophysiological markers of early recurrence after ventricular fibrillation defibrillation after myocardial infarction and the therapeutic effect of renal sympathetic nerve removal and its potential mechanism [25]. Through rational animal selection, experimental operation and data analysis, we successfully accomplished the experimental objectives and obtained meaningful research results. In the experimental protocol, we selected adult male Sprague-Dawley rats as experimental subjects, and underwent myocardial infarction induction and ventricular fibrillation defibrillation treatment. We recorded electrocardiogram signals in post-defibrillation rats and analyzed the association between electrophysiological markers and the risk of early recurrence. At the same time, we performed a therapeutic intervention to remove the sympathetic nerve around the renal artery by surgical removal. By assessing ECG, cardiac function, and neurotransmitters, we evaluated the effect of renal sympathetic removal on the recurrence of ventricular fibrillation [26].

Although the experimental protocol of this study has been detailed and scientific, there are still some improvements: (1) Larger sample size: Increasing the sample size can improve the statistical power and reliability of experimental results and reduce the impact of accidental error. (2) Consideration of different dosages and time points: In the experimental protocol, specific drug dosages and surgical time points were used; however, future studies may consider variations in different dosages and time points to further evaluate therapeutic effects and dose dependence. (3) Feasibility study of clinical transformation: This study mainly focuses on experimental studies on animal models, providing preliminary basis for further clinical transformation. Future studies require more clinical trials and human studies to verify the feasibility and applicability of the experimental results [27].

This study has important clinical significance for the risk assessment and individualized treatment of early recurrence of ventricular fibrillation after defibrillation after myocardial infarction: Through the analysis of electrophysiological markers, the risk of early recurrence of ventricular fibrillation after myocardial infarction can be predicted, which is helpful to take timely intervention measures to avoid recurrence. By removing the sympathetic nerve in the kidney, therapeutic interventions can improve the stability and function of the heart and reduce the risk of early recurrence. This provides a new strategy and method for individualized treatment. The results of this study provide a new idea and target for the treatment and prevention of ventricular fibrillation after myocardial infarction. In the future, based on these findings, further clinical trials could be conducted to explore incorporating renal sympathetic nerve removal into clinical practice for the treatment of ventricular fibrillation. The experimental scheme of this study has been reasonably designed and strictly implemented, which provides

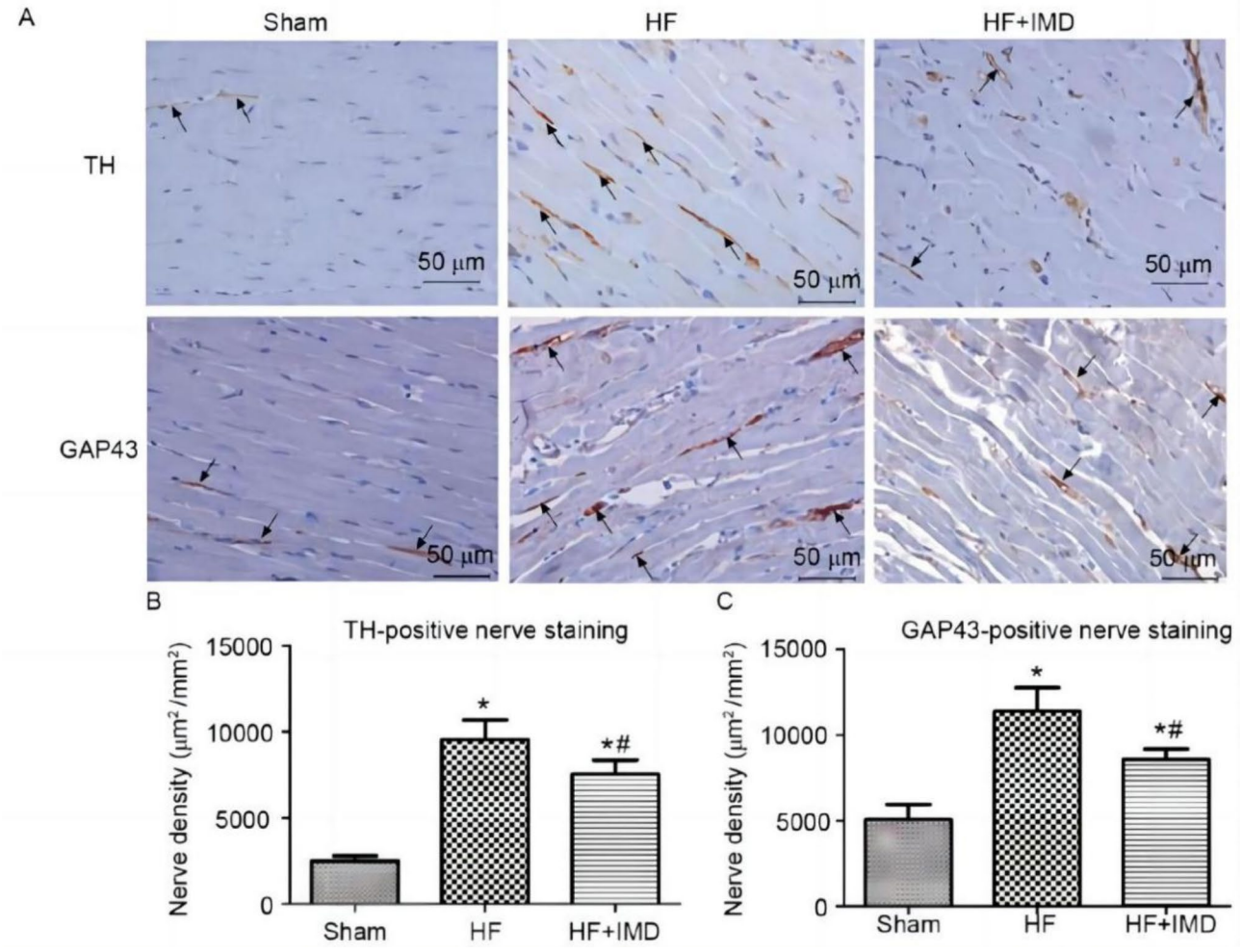

Fig. 7 Pathologic features of renal sympathetic nerve removal after ventricular fibrillation after myocardial infarction

a reliable experimental basis for the realization of the research objectives. At the same time, the results of this study have important clinical significance, and provide a new direction for the risk assessment and individualized treatment of ventricular fibrillation after myocardial infarction. However, further improvements to experimental protocols and more clinical studies are needed to validate and apply these findings [28].

In summary, this study explored the relationship between the electrophysiological markers of early relapse after ventricular fibrillation defibrillation after myocardial infarction and the therapeutic effect of renal sympathetic nerve removal and its potential mechanism. The results of this study provide an important basis for the risk assessment and individualized treatment of ventricular fibrillation after myocardial infarction. However, further clinical and mechanistic studies are needed to validate and refine these results. Future studies can further expand the scope of electrophysiological markers and further study the therapeutic mechanism combined with molecular biology techniques to provide more effective strategies for the prevention and treatment of ventricular fibrillation.

Conclusion

The de-sympathetic intervention strategy may have potential cardiac electrophysiological modulatory effects that are beneficial in preventing or treating electrophysiological abnormalities in similar model groups and may be beneficial in preventing arrhythmias and increasing the threshold for ventricular fibrillation. This measure had a positive effect on improving the electrophysiological properties of cardiac cells and may provide a new strategy for treating related cardiac diseases.

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Xiaowei qiu designed the study. Caixia Lin collected raw data and wrote the original draft. Zhengyu Feng performed statistical and bioinformatics analyses. Xiaowei qiu supervised the study. All authors read and approved the final version of the manuscript.

Author contributions

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethical approval
Confirm that all methods are reported in accordance with ARRIVE guidelines (https://arriveguidelines.org) for the reporting of animal experiments. this study protocol was approved by the Ethics Committee of Ruijin Hospital Luwan Branch, Shanghai Jiao Tong University (NO.20200819 S).

Informed consent
Informed consent was obtained from all patients.

Competing interests
The authors declare no competing interests.

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References

1. Garcia R, Marijon E, Karam N, et al. Ventricular fibrillation in acute myocardial infarction: 20-year trends in the FAST-MI study. Eur Heart J. 2022;43(47):4887–96.
2. Weizman O, Marijon E, Narayanan K, et al. FAST-MI program investigators. Incidence, characteristics, and outcomes of ventricular fibrillation complicating Acute myocardial infarction in women admitted alive in the hospital. J Am Heart Assoc. 2022;11(17):e025959.
3. Julian DG, Campbell RW, Murray A. Predicting and preventing ventricular fibrillation in acute myocardial infarction. Adv Cardiol. 1978;25:183–90.
4. Hundahl LA, Tfelt-Hansen J, Jespersen T. Rat models of ventricular fibrillation following Acute myocardial infarction. J Cardiovasc Pharmacol Ther. 2017;22(6):514–28.
5. Holmstrom L, Chugh SS. How to minimize in-hospital mortality from acute myocardial infarction: focus on primary prevention of ventricular fibrillation. Eur Heart J. 2022;43(47):4897–8.
6. Dewhurst NG, Hannan WJ, Muir AL. Ventricular performance and prognosis after primary ventricular fibrillation complicating acute myocardial infarction. Eur Heart J. 1984;5(4):275–81.
7. Nordrehaug JE, von der Lippe G. Hypokalaemia and ventricular fibrillation in acute myocardial infarction. Br Heart J. 1983;50(6):525–9.
8. Galcerá-Jornet E, Consuegra-Sánchez L, Galcerá-Tomás J, et al. Association between new-onset right bundle branch block and primary or secondary ventricular fibrillation in ST-segment elevation myocardial infarction. Eur Heart J Acute Cardiovasc Care. 2021;10(8):918–25.
9. Flugelman MY, Flugelman AA, Rozenman J, et al. Prediction of atrial and ventricular fibrillation complicating myocardial infarction from admission data: a prospective study. Clin Cardiol. 1987;10(9):503–5.
10. Liang JJ, Prasad A, Cha YM. Temporal evolution and implications of ventricular arrhythmias associated with acute myocardial infarction. Cardiol Rev. 2013 Nov-Dec;21(6):289–94.
11. Kiuchi MG, Chen S, Silva GR E, Rodrigues Paz LM, Kiuchi T, de Paula Filho AG, Lima Souto GL. The addition of renal sympathetic denervation to pulmonary vein isolation reduces recurrence of paroxysmal atrial fibrillation in chronic kidney disease patients. J Interv Card Electrophysiol. 2017;48(2):215–22.
12. Indik JH, Donnerstein RL, Berg RA, et al. Ventricular fibrillation frequency characteristics are altered in acute myocardial infarction. Crit Care Med. 2007;35(4):1133–8.
13. Wu L, Zheng Y, Liu J, et al. Comprehensive evaluation of the efficacy and safety of LPV/r drugs in the treatment of SARS and MERS to provide potential treatment options for COVID-19. Aging. 2021;13(8):10833–52.
14. Klotzka A, Iwańczyk S, Smukowski T, et al. Idiopathic ventricular fibrillation or myocardial infarction? The impact of optical coherence tomography on therapeutic decisions. Kardiol Pol. 2020;78(11):1176–7.
15. Wyman MG, Wyman RM, Cannom DS, et al. Prevention of primary ventricular fibrillation in acute myocardial infarction with prophylactic lidocaine. Am J Cardiol. 2004;94(5):545–51.
16. Geuze RH, Koster RW. Ventricular fibrillation and transient arrhythmias after defibrillation in patients with acute myocardial infarction. J Electrocardiol. 1984;17(4):353–60.
17. Behar S, Kishon Y, Reicher-Reiss H, et al. Prognosis of early versus late ventricular fibrillation complicating acute myocardial infarction. Int J Cardiol. 1994;45(3):191–8.
18. Wu L, Zhong Y, Yu X, et al. Selective poly adenylation predicts the efficacy of immunotherapy in patients with lung adenocarcinoma by multiple omics research. Anticancer Drugs. 2022;33(9):943–59.
19. Volpi A, Cavalli A, Santoro E, et al. Incidence and prognosis of secondary ventricular fibrillation in acute myocardial infarction. Evidence for a protective effect of thrombolytic therapy. GISSI Investigators Circulation. 1990;82(4):1279–88.
20. Zhang Y, Wang J, Xu Y. Value of heart rate variability on dynamic electrocardiogram in predicting ventricular fibrillation in elderly acute myocardial infarction patients. Ann Palliat Med. 2020;9(5):3488–94.
21. Azarov JE, Demidova MM, Koul S, et al. Progressive increase of the Tpeak-Tend interval is associated with ischaemia-induced ventricular fibrillation in a porcine myocardial infarction model. Europace. 2018;20(5):880–6.
22. Rudic B, Veltmann C, Kuntz E, et al. Early repolarization pattern is associated with ventricular fibrillation in patients with acute myocardial infarction. Heart Rhythm. 2012;9(8):1295–300.
23. Wang W, Chen QF, Yin RX, et al. Clinical features, risk factors, and treatment experience: a review of 74 patients with ST-segment elevation myocardial infarction complicated by ventricular fibrillation. J Emerg Med. 2014;47(6):729–35.
24. Forssell G, Orinius E. QT prolongation and ventricular fibrillation in acute myocardial infarction. Acta Med Scand. 1981;210(4):309–11.
25. Goldman L, Batsford WP. Risk-benefit stratification as a guide to lidocaine prophylaxis of primary ventricular fibrillation in acute myocardial infarction: an analytic review. Yale J Biol Med. 1979 Sep-Oct;52(5):455–66. PMID: 392960; PMCID: PMC2595788.
26. Indik JH, Allen D, Gura M, et al. Utility of the ventricular fibrillation waveform to predict a return of spontaneous circulation and distinguish acute from post myocardial infarction or normal swine in ventricular fibrillation cardiac arrest. Circ Arrhythm Electrophysiol. 2011;4(3):337–43.
27. Chevalier P, Moreau A, Bessière F, et al. MAP-IDM investigators. Identification of Cx43 variants predisposing to ventricular fibrillation in the acute phase of ST-elevation myocardial infarction. Europace. 2023;25(1):101–11.
28. Martinez-Rubio A, Shenasa M, Borggrefe M, et al. Electrophysiologic variables characterizing the induction of ventricular tachycardia versus ventricular fibrillation after myocardial infarction: relation between ventricular late potentials and coupling intervals for the induction of sustained ventricular tachyarrhythmias. J Am Coll Cardiol. 1993;21(7):1624–31.

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