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Article

AKAP1 in Renal Patients with AHF to Reduce Ferroptosis of Cardiomyocyte

Yifeng Fang[1,*], Junpeng Xu[1], Ruofei Huang[2]

[1]Department of Emergency, The First People's Hospital of Yongkang, 321390 Yongkang, Zhejiang, China
[2]Department of Endocrine, The First People's Hospital of Yongkang, 321390 Yongkang, Zhejiang, China
*Correspondence: yifengfang@yeah.net (Yifeng Fang)

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Abstract

Background: This study mainly investigated the mechanism and effects of AKAP1 in renal patients with acute heart failure (AHF). **Methods**: Patients with renal patients with AHF and normal volunteers were collected. The left anterior descending arteries (LAD) of mice were ligated to induce myocardial infarction. **Results**: AKAP1 messenger RNA (mRNA) expression was found to be down-regulated in renal patients with AHF. The serum levels of AKAP1 mRNA expression were negatively correlated with collagen I/III in patients. AKAP1 mRNA and protein expression in the heart tissue of mice with AHF were also found to be down-regulated in a time-dependent manner. Short hairpin (Sh)-AKAP1 promotes AHF in a mouse model. AKAP1 up-regulation reduces reactive oxygen species (ROS)-induced oxidative stress in an *In Vitro* model. AKAP1 up-regulation also reduces ROS-induced lipid peroxidation ferroptosis in an *In Vitro* model. AKAP1 induces NDUFS1 expression to increase GPX4 activity levels. AKAP1 protein interlinked with the NDUFS1 protein. Up-regulation of the *AKAP1* gene reduced NDUFS1 ubiquitination, while down-regulation of the *AKAP1* gene increased NDUFS1 ubiquitination in a model. *In vivo* imaging showed that the sh-AKAP1 virus reduced NDUFS1 expression in the heart of a mouse model. **Conclusions**: AKAP1 reduced ROS-induced lipid peroxidation ferroptosis through the inhibition of ubiquitination of NDUFS by mitochondrial damage in model of renal patients with AHF, suggest a novel target for AHF treatment.

Keywords

AKAP1; AHF; chronic kidney disease; NDUFS; ferroptosis

Introduction

Acute heart failure (AHF) is a common type of cardiovascular disease in clinical practice [1,2]. Acute attacks or exacerbations can lead to abnormal cardiac function, continuously increasing cardiac load, and in severe cases, can lead to classic symptoms such as syncope and shock, posing a threat to the patient's life safety [2]. In clinical practice, changes in the levels of multiple serum markers can affect the patient's condition [3]. It is necessary to give timely diagnosis and targeted treatment to stabilize the hemodynamic state of the body and improve clinical symptoms, so as to stabilize the patient's condition, reduce the incidence rate, recurrence rate and mortality rate [3].

Chronic kidney disease (CKD) patients generally have a low-intensity, persistent inflammatory and oxidative state in their bodies, known as microinflammation [4]. Clinical studies have found that anti-inflammatory and antioxidant treatments in CKD patients can reduce major adverse cardiovascular events [5]. Inflammation and reactive oxygen species (ROS) production may play a role in AHF in CKD patients [6,7]. Patients can show typical symptoms such as dyspnea, wheezing, fatigue, *etc*. Their condition can be diagnosed and evaluated in accordance with the basic causes, clinical symptoms, electrocardiogram (ECG) examination, *etc*., and evaluate the prognosis of patients, as different patients have different physical constitution and severity of the disease, resulting in certain differences in prognosis recovery [6,7].

AHF is a common cardiac circulatory dysfunction syndrome in clinical practice. Severe illness can lead to patient death in a short period of time, posing a serious threat to patient safety [8]. At the same time, iron participates in the activation of lipoxygenase (LOX), promoting the generation of lipid peroxides and leading to iron death [9]. In addition, iron accumulation caused by NCOA4-mediated ferritin phagocytosis can accelerate the process of iron death [9,10]. Cardiomyocytes are non-regenerative, and once damaged or necrotic, they will further affect function of the heart, exacerbating the deterioration of AHF [9]. AHF and tachyarrhythmias are a vicious cycle, and the condition progresses rapidly. Patients have systolic and diastolic dysfunction, decreased cardiac function, and are prone to various complications, leading to further deterioration of the condition. After the occurrence of AHF, there is a significant decrease in cardiac ejection, resulting in insufficient blood perfusion of organs and various complica-

tions such as tachyarrhythmia. Therefore, anti-heart failure and anti-arrhythmia treatment are necessary for AHF and tachyarrhythmia [9]. The commonly used drugs for clinical treatment of AHF and tachyarrhythmia, *etc*. However, these antiarrhythmic drugs are prone to negative muscle strength, which limits their clinical application [9].

AKAP1 is a scaffold protein that is fixed on the outer membrane of mitochondria and is involved in mitochondrial proliferation and dynamics [11]. Studies have shown that AKAP1 can integrate cAMP signals to regulate organelle biosynthesis [12,13]. In the human placenta, AKAP1 can regulate the protein expression and activity of PKA, promote progesterone synthesis, and progesterone is an intermediate product of testosterone synthesis [14]. In addition, AKAP1 can also promote the transcription level of StAR protein, promote the translocation of cholesterol into mitochondria, and further stimulate the secretion of testosterone [14]. Research has shown that AKAP1 regulates DRP1-dependent mitochondrial fission driven by PTEN-induced kinase 1 (PINK1) and further induces mitochondrial autophagy [15]. In addition, there is also research indicating that AKAP1 usually regulates cAMP-dependent PKA activity and mitochondrial dynamics through the ubiquitination degradation pathway [16]. This study mainly investigated the mechanism and effects of AKAP1 in renal patients with AHF.

Materials and Methods

Model for Clinical Research

Patients with renal patients with AHF and normal volunteers (Number = 26) were collected from our hospital (No. 20200506L161). Experimental protocols were approved by our hospital. Each candidate patient provided their written informed consent for study participation.

Animals Model of AHF

All aspects of the animal care and experimental protocols were approved by the Committee on Animal Care of our hospital (No. 20210312M023). Mice were ventilated by a rodent ventilator (Shanghai Alcott Biotech Co., Shanghai, China), then left anterior descending arteries (LAD) was ligated by an 8.0 suture followed by the thoracotomy as literature [17]. At 2 weeks of modeling, mice were sacrificed and executed other experiment. Left ventricular stroke volume (LVSV), left ventricular ejection fraction (LVEF), and left ventricular fractional shortening (LVFS), while enhancing left ventricular internal diameter (LVID) were obtained from Nillar pressure-volume system (MPVS-400, shanghai, China). Mice were anesthetized using 50 mg/kg of pentobarbital sodium (MedChemExpress, shanghai, China), and then sacrificed using cervical dislocation method for execution.

Vitro Experimental Design

H9c2 cells were performed transfections using Lipofectamine 2000 (Shanghai, China, Thermo Fisher Scientific). Plasmid (GGGAGCAUGUCUUGGAAUU) or small interfering (si)-AKAP1RNAs (sc-270134, Santa Cruz Biotechnology) were transfected in H9c2 cells (GNR 5, Cell Bank of Typical Culture Preservation Committee of Chinese Academy of Sciences). After 48 h of transfection, H9c2 cells were stimulated with 1% oxygen (O_2) and 5% carbon dioxide (CO_2) and 95% N_2 for 4 h as literature [18,19]. Subsequently, plates were removed to a normoxic chamber for 2 h to establish reoxygenation.

ELISA Kits, Histological Analysis and Immunohistochemistry

ROS production (S0033S), malondialdehyde (MDA) (S0131S), superoxide dismutase (SOD) (S0101S), glutathione (GSH) (S0053), glutathione peroxidase (GSH-px) (S0059S) kits (Beyotime, Nanjing, China) were used to measure the cytokine levels as business brochure (Beyotime) as related literature [17]. Tissue samples were fixed in 4% paraformaldehyde, and executed histological analysis and immunohistochemistry according to references [20,21].

Real-Time PCR

Total RNAs were isolated with RNA extraction reagent (Takara, Dalian, China) and complementary DNA (cDNA) was synthesized using PrimeScipt RT Master Mix (Takara, Dalian, China). qPCR were performed with the Prime-ScriptTM RT detection kit. Relative levels of the sample messenger RNA (mRNA) expression were calculated and expressed as 2-DDCt. AKAP1: Forward: 5′-CCTTGCCGAAGATCAGAGTCC-3′, Reverse: 5′-TGCTGGAGAATAGTACACCCTTT-3′; GAPDH: Forward: 5′-GGAGTCCACTGGCGTCTTCA-3′, Reverse: 5′-GTCATGAGTCCTTCCACGATACC-3′.

Western Blot

Western blot was performed as previously described [22]. Membranes were incubated with AKAP1 (ab156004, 1:1000, Abcam, shanghai, China), NDUFS1 (ab169540, 1:1000, Abcam, shanghai, China), GPX4 (ab125066, 1:1000, Abcam, shanghai, China) and β-Actin (BS6007MH, 1:5000, Bioworld Technology, Inc., Shanghai, China) at 4 °C overnight. The membranes were incubated with horseradish peroxidase-conjugated secondary antibodies (ab205718, 1:5000, Abcam, shanghai, China; ab131368, 1:5000, Abcam, shanghai, China) for 1 h at 37 °C after washing with TBST (servicebio, Wuhan, China) for 15 min. Protein was measured using an enhanced chemilu-

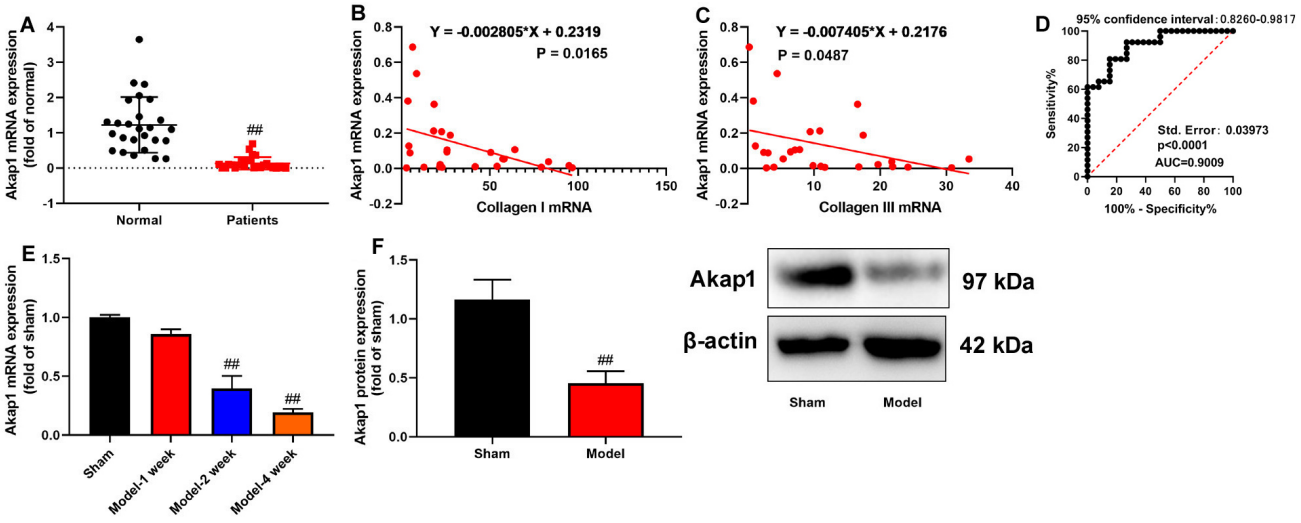

Fig. 1. Prognostic value of AKAP1 in renal patients with acute heart failure (AHF). The serum AKAP1 messenger RNA (mRNA) expression (A) was positive correlation with collagen I and collagen III mRNA expression (B,C), reactive oxygen species (ROS) curve (D) in patients; AKAP1 mRNA and protein expression in mice model (E,F). $^{\#\#}p < 0.01$ compared with normal or sham group.

minescence system (ECL, Beyotime, Nanjing, China) and analyzed using an Image Lab 3.0 (Bio-Rad Laboratories, Inc., Shanghai, China).

Statistical Analysis

Data were represented as mean ± standard error of the mean (SEM). Student's *t* test and one way ANOVA test by Duncan's post hoc test were used for statistical analyses of the data. A *p*-value less than 0.05 is considered with significant difference.

Results

AKAP1 in Patients with AHF

This study aimed to investigate the prognostic value of AKAP1 in patients with AHF. The serum levels of AKAP1 mRNA expression were found to be down-regulated in patients with AHF (Fig. 1A). The serum levels of AKAP1 mRNA expression were negatively correlated with collagen I/III in patients (Fig. 1B,C). A receiver operating characteristic (ROC) curve was constructed to assess the diagnostic value of AKAP1 in renal patients with AHF (Fig. 1D). Furthermore, AKAP1 mRNA and protein expression in the heart tissue of mice with AHF were also found to be down-regulated in a time-dependent manner (Fig. 1E,F). AKAP1 may have diagnostic and predictive value in patients with kidney disease and AHF.

Inhibition of AKAP1 Promotes AHF in a Mouse Model

Based on the above results, we further examined the function of AKAP1 in a mouse model of AHF, sh-AKAP1 virus was induced into mice with AHF. The results showed that sh-AKAP1 virus increased creatine kinase (CK) and lactate dehydrogenase (LDH) activity levels, inhibited myocardial fibrosis, and reduced LVSV, LVEF, and LVFS, while enhancing LVID in the model of AHF (Fig. 2A–G). Sh-AKAP1 virus also promoted the mRNA expression of collagen I/III, and TGF-β1, increased MDA levels, and reduced SOD, GSH, and GSH-px levels in the model of AHF (Fig. 2H–O). The inhibition of AKAP1 accelerated AHF through oxidative stress in mice model.

AKAP1 Up-Regulation Reduces Oxidative Stress in an In Vitro Model

In mouse models, AKAP1 has been shown to modulate oxidative stress, we investigated the effects of AKAP1 on oxidative stress in an *in vitro* model of acute myocardial infarction (AMI), AKAP1 plasmid was used to up-regulate AKAP1 mRNA expression (Fig. 3A). *AKAP1* gene reduced oxidative stress in the *in vitro* model of AMI (Fig. 3B–F). In contrast, down-regulation of AKAP1 using si-AKAP1 mimics increased oxidative stress in the *in vitro* model of AMI (Fig. 3G–L). Moreover, *AKAP1* gene reduced collagen I/III mRNA expression in the *in vitro* model (Fig. 3M,N), while *AKAP1* gene down-regulation increased collagen I/III mRNA expression in the *in vitro* model (Fig. 3O,P). So, AKAP1 up-regulation reduced oxidative stress of cardiomyocyte *in vitro* model.

AKAP1 Up-Regulation Reduces Lipid Peroxidation Ferroptosis in an In Vitro Model

The effects of AKAP1 on ferroptosis in an *in vitro* model of heart failure were also evaluated. *AKAP1* gene up-regulation increased cell growth, reduced LDH activity lev-

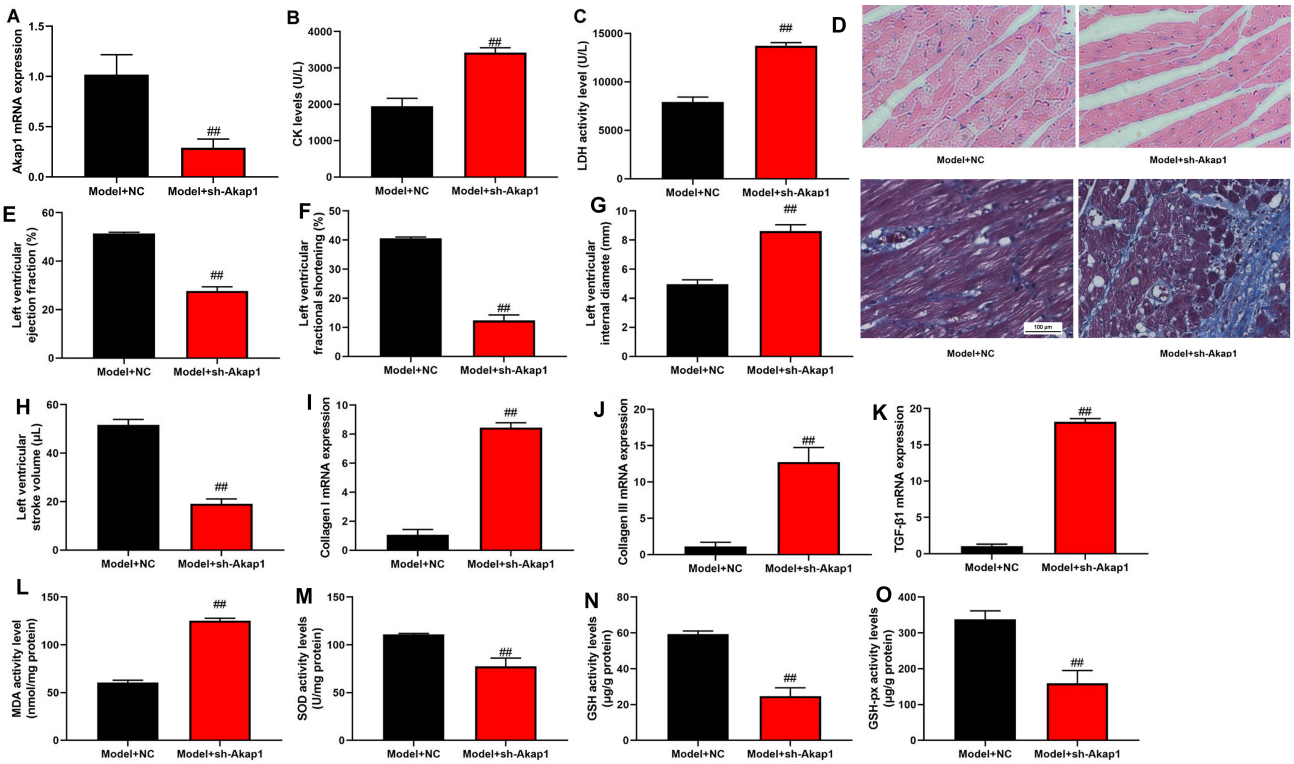

Fig. 2. Sh-AKAP1 promoted AHF in model of mice. Creatine kinase (CK) and lactate dehydrogenase (LDH) activity (A,B), myocardial fibrosis (HE staining/Masson staining (C)), left ventricular ejection fraction, scale bar, 100 μm (D), left ventricular stroke volume (E), left ventricular internal diameter (F), ventricular fractional shortening (G), collagen I/III and TGF-β1 mRNA expression (H–J), malondialdehyde (MDA)/superoxide dismutase (SOD)/glutathione (GSH)/glutathione peroxidase (GSH-px) levels (K–O). $^{\#\#}p < 0.01$ compared with model + NC group.

els, propidium iodide (PI)-positive cells, and iron content, improved JC-1 levels and membrane permeability transition (MPT), and restored mitochondrial structure in the *in vitro* model (Fig. 4A–G). In contrast, *AKAP1* gene down-regulation reduced cell growth, increased LDH activity levels, PI-positive cells, and iron content, inhibited JC-1 levels and MPT, and destroyed mitochondrial structure in the *in vitro* model (Fig. 4H–N). Sh-AKAP1 virus was found to suppress GPX4 mRNA and protein expression in the model mice (Fig. 4O,P). Furthermore, *AKAP1* gene induced GPX4 protein expression, while si-*AKAP1* gene suppressed GPX4 protein expression in the *in vitro* model (Fig. 4Q,R). Therefore, AKAP1 reduced ferroptosis of cardiomyocyte *in vitro* model through the inhibition of ROS-induced lipid peroxidation.

AKAP1 Induces NDUFS1 Expression to Increase GPX4 Activity Levels

The above results show that AKAP1 has the ability to reduce ferroptosis, but the mechanism is still unclear. The study investigated the anti-ferroptosis mechanism of AKAP1 in renal patients with AHF. *AKAP1* gene induced AKAP1 and NDUFS1 protein expressions, while down-regulation of the *AKAP1* gene suppressed AKAP1 and NDUFS1 protein expressions in an *in vitro* model (Fig. 5A,B). Meanwhile, the sh-AKAP1 virus suppressed NDUFS1 protein expression in a mouse model (Fig. 5C). *AKAP1* gene increased AKAP1 and NDUFS1 expressions in an *in vitro* model (Fig. 5D). *In vivo* imaging showed that the sh-AKAP1 virus reduced NDUFS1 expression in the heart of a mouse model (Fig. 5E). Next, AKAP1 protein interlinked with the NDUFS1 protein (Fig. 5F). Up-regulation of the *AKAP1* gene reduced NDUFS1 ubiquitination, while down-regulation of the *AKAP1* gene increased NDUFS1 ubiquitination in a model (Fig. 5G). To summarize, AKAP1 induces the expression of NDUFS1, which subsequently increases the activity levels of GPX4. This increase in GPX4 activity levels leads to a reduction in ferroptosis of cardiomyocytes in the model of AHF.

The Inhibition of NDUFS1 Reduced the Function of AKAP1 on ROS-Induced Lipid Peroxidation Ferroptosis in an In Vitro Model

The above results indicate that AKAP1 may regulate NDUFS1 to achieve the function of regulating ferroptosis. This experiment further investigated the role of NDUFS1 in the function of AKAP1 on ROS-induced lipid peroxidation ferroptosis in an *in vitro* model. The NDUFS1 plas-

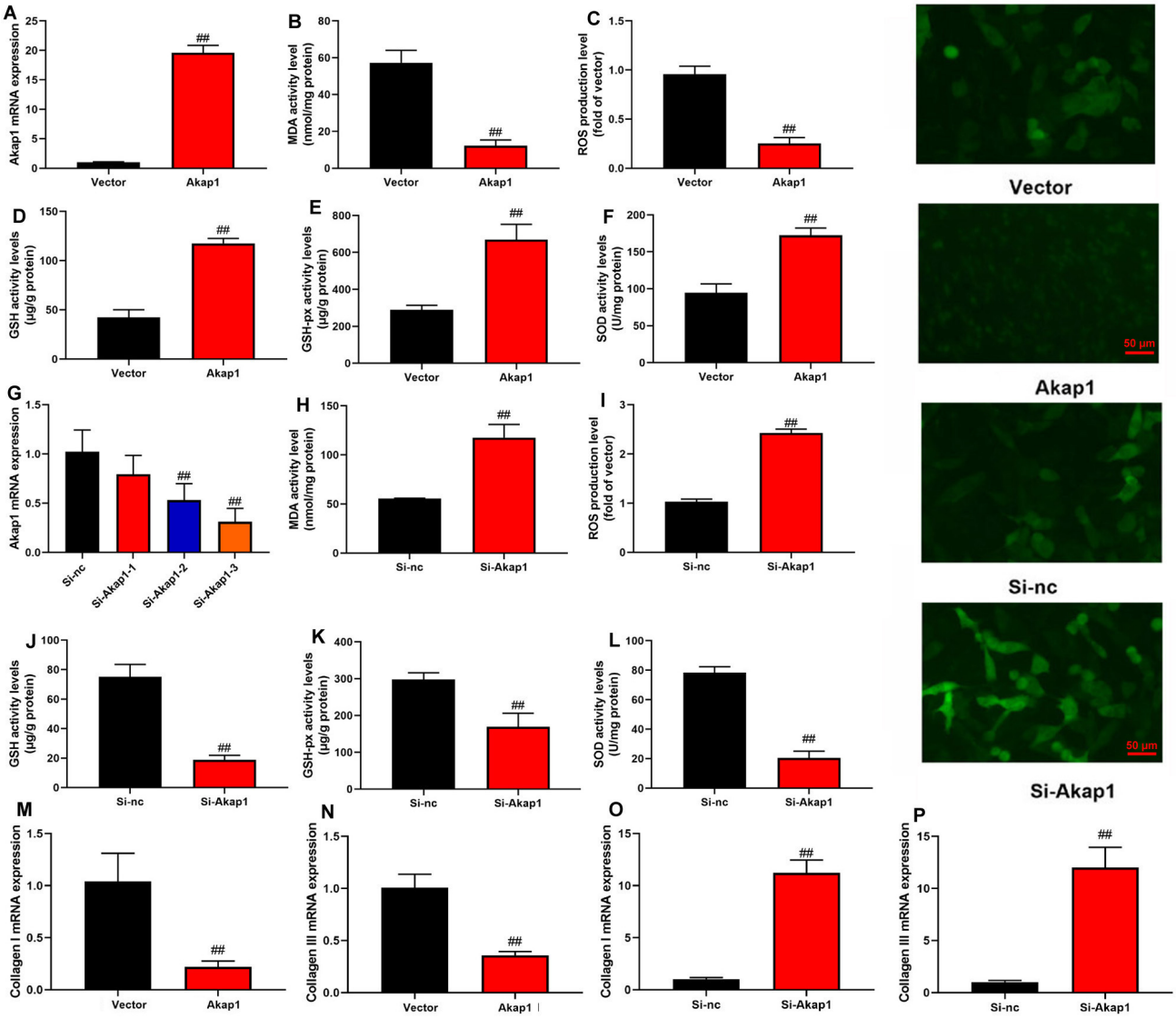

Fig. 3. AKAP1 up-regulation reduced ROS-induced oxidative stress *in vitro* model. AKAP1 mRNA expression (A), MDA/ROS/GSH/GSH-px/SOD levels (B–F), AKAP1 mRNA expression (G), MDA/ROS/GSH/GSH-px/SOD levels (H–L), collagen I and collagen III mRNA expression (M,N) *in vitro* model by AKAP1 up-regulation; collagen I and collagen III mRNA expression (O,P) *in vitro* model by AKAP1 down-regulation. $^{\#\#}p < 0.01$ compared with negative control group or si-negative control group.

mid induced NDUFS1 and GPX4 protein expressions in an *in vitro* model by AKAP1 down-regulation (Fig. 6A). Up-regulation of NDUFS1 increased cell growth, reduced LDH activity levels, PI-positive cells, and iron content, improved JC-1 levels and MPT, and recovered mitochondrial structure in an *in vitro* model by AKAP1 down-regulation (Fig. 6B–H). Si-NDUFS1 suppressed NDUFS1 and GPX4 protein expressions in an *in vitro* model by AKAP1 up-regulation (Fig. 6I). Down-regulation of NDUFS1 reduced cell growth, increased LDH activity levels, PI-positive cells, and iron content, inhibited JC-1 levels and MPT, and destroyed mitochondrial structure in an *in vitro* model by AKAP1 up-regulation (Fig. 6J–P).

NDUFS1 down-regulation increased oxidative stress and collagen I/III mRNA expression in an *in vitro* model by AKAP1 up-regulation (Fig. 7A–G). Up-regulation of NDUFS1 also reduced oxidative stress and collagen I/III mRNA expression in an *in vitro* model by AKAP1 down-regulation (Fig. 7H–N). AKAP1 may target NDUFS1 to regulate ferroptosis in a model of AHF.

Discussion

Its clinical symptoms mainly include dyspnea, limited movement and water retention. The pathogenesis of chronic heart failure is a complex process involving multiple factors, with oxidative stress and ferroptosis playing a crucial role. In the human body, in addition to the oxidation system, there is also an effective antioxidant defense

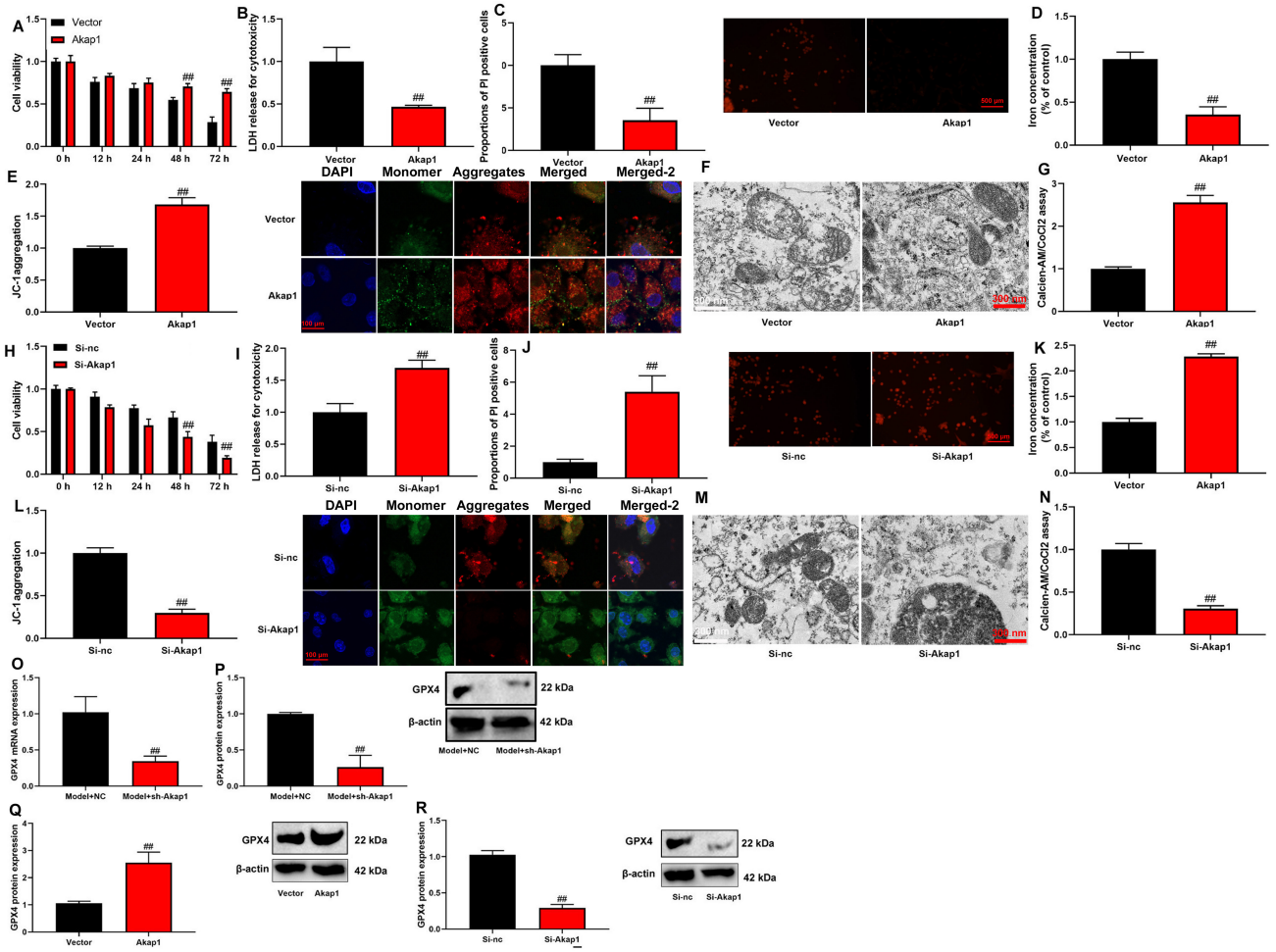

Fig. 4. AKAP1 up-regulation reduced ROS-induced lipid peroxidation ferroptosis *in vitro* model. Cell viability (A), LDH activity levels (B), PI-positive cells (C), Iron concentration (D), JC-1 levels (E), mitochondrial structure (F), MPT (G) *in vitro* model by AKAP1 up-regulation; Cell viability (H), LDH activity levels (I), propidium iodide (PI)-positive cells (J), Iron concentration (K), JC-1 levels (L), mitochondrial structure (M), membrane permeability transition (MPT) (N) *in vitro* model by AKAP1 down-regulation; GPX4 mRNA and protein expression in the model mice (O,P), GPX4 protein expression (Q,R). $^{\#\#}p < 0.01$ compared with negative control group or si-negative control group or model + NC group.

system. The oxygen in the heart and its metabolic pathways are unusually complex. Overactivation of peroxidation and excessive accumulation of lipid peroxides lead to intracellular homeostasis imbalance. The activation of the iron homeostasis regulatory pathway leads to the aggregation of iron ions, leading to the occurrence of oxidative damage mediated by iron ions, indicating that the mechanism of ferroptosis is involved in myocardial injury. When ROS is not cleared by antioxidants in time and accumulated excessively, a large amount of malondialdehyde (MDA), a highly toxic lipid peroxidation product, will be produced, which can further aggravate the oxidative stress reaction and intima damage. As an important metal antioxidant enzyme in the antioxidant system, superoxide dismutase (SOD) can be an important substance for scavenging oxygen free radicals, SOD can catalyze ROS to produce disproportionation reaction, thus eliminating oxygen free radicals to reduce damage to tunica intima. Under some pathological conditions, the heart can lead to excessive accumulation of iron, and pathological changes in membrane lipids. These changes in antioxidant and lipid peroxides are important factors for ferroptosis. ROS related oxidative stress reactions can regulate ferroptosis of chronic heart failure. But the specific regulatory mechanisms still need to be studied [23]. CKD patients often have sustained inflammation [24]. Timely assessment and monitoring of inflammation levels in CKD patients are of great significance for predicting and developing AHF [25]. We found that AKAP1 promoted AHF in model of mice Inhibiting AKAP1 was found to promote AHF in a mouse model through oxidative stress. Wang *et al.* [26] demonstrated that AKAP1 deficiency promoted fatty acid oxidation in brown adipocytes. These data indicated that AKAP1 participated in the ROS-induced oxidative stress of AHF. AKAP1 exerts a regulatory role in

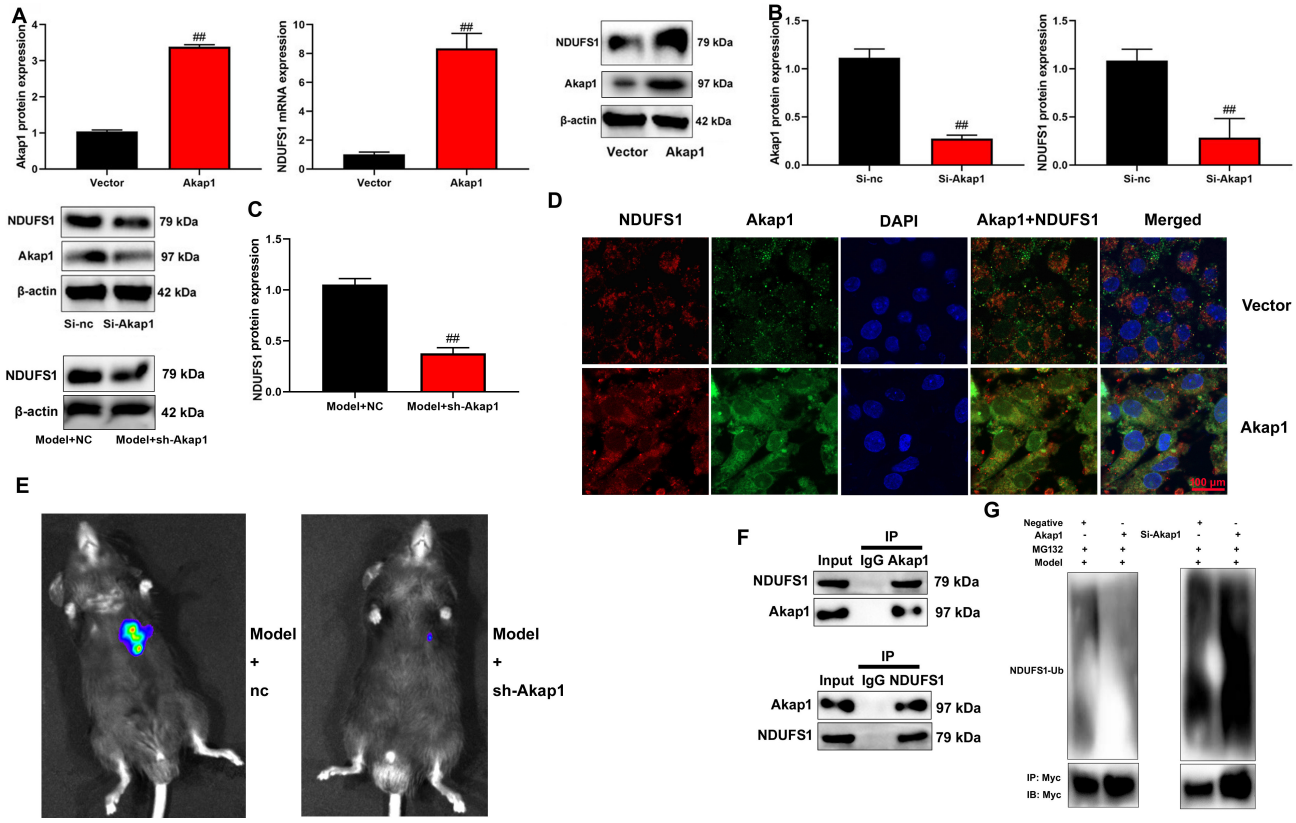

Fig. 5. AKAP1 induced NDUFS1 expression to increase GPX4 activity level. AKAP1/NDUFS1 protein expression (A,B) *in vitro* model, NDUFS1 protein expression in mice model (C), AKAP1/NDUFS1 expression (confocal microscope, D), NDUFS1 expression in heart of model of mice (vivo imaging, E), AKAP1 protein interlinked with NDUFS1 protein (F), PFKFB3 ubiquitination (G), $^{\#\#}p < 0.01$ compared with negative control group or si-negative control group or model + NC group.

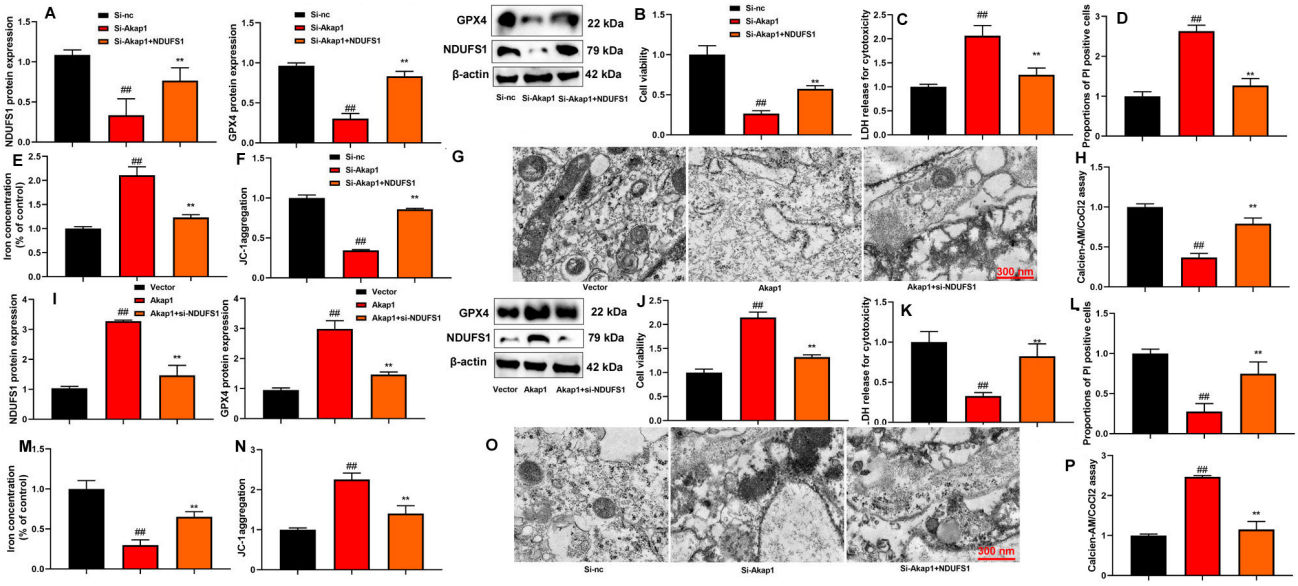

Fig. 6. The inhibition of NDUFS1 reduced the function of AKAP1 on ferroptosis *in vitro* model. NDUFS1/GPX4 protein expression (A), Cell growth (B), LDH activity levels (C), PI-positive cells (D), iron content (E), JC-1 levels (F), mitochondrial structure (G), MPT (H) *in vitro* model by si-AKAP1 + NDUFS1; NDUFS1/GPX4 protein expression (I), cell growth (J), LDH activity levels (K), PI-positive cells (L), iron content (M), JC-1 levels (N), mitochondrial structure (O), MPT (P) *in vitro* model by AKAP1 + si-NDUFS1. $^{\#\#}p < 0.01$ compared with negative control group or si-negative control group; $^{**}p < 0.01$ compared with AKAP1 group or si-AKAP1 group.

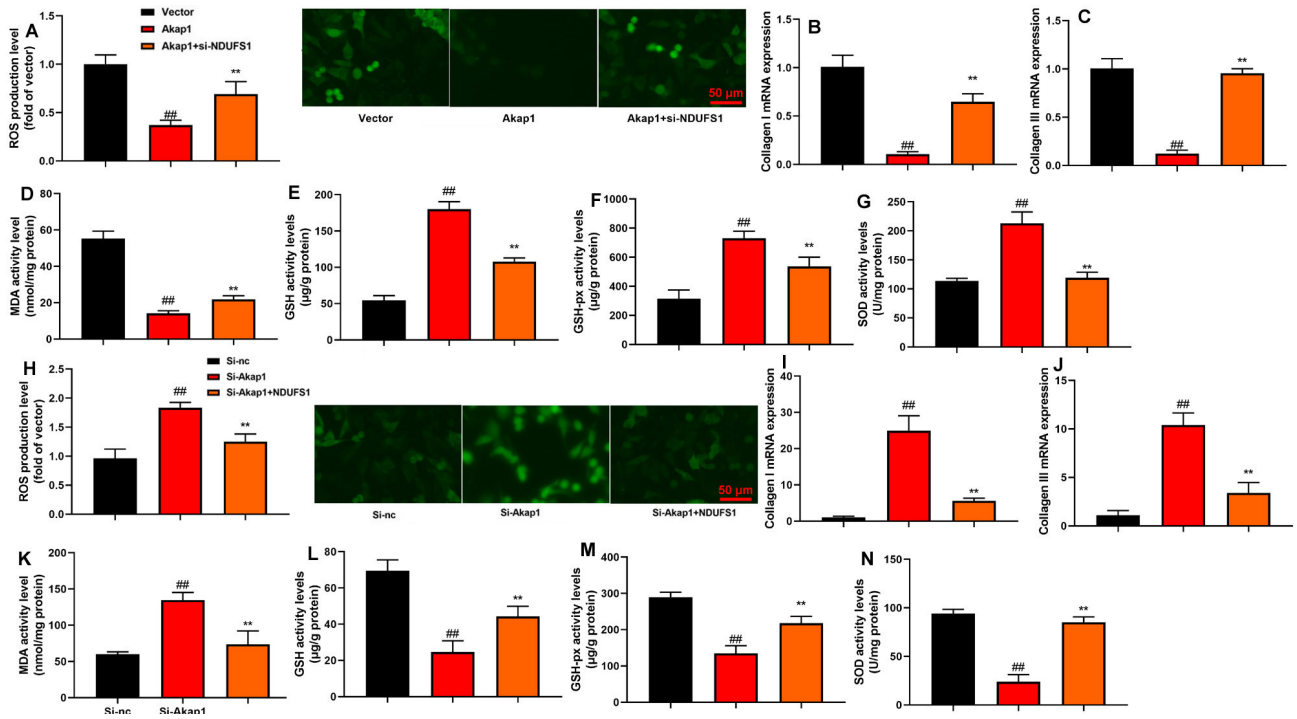

Fig. 7. The inhibition of NDUFS1 reduced the function of AKAP1 on ROS-induced lipid peroxidation *in vitro* model. ROS (A), collagen I and collagen III mRNA expression (B,C), MDA/GSH/GSH-px/SOD levels (D–G) *in vitro* model by AKAP1 + si-NDUFS1; ROS (H), collagen I and collagen III mRNA expression (I,J), MDA/GSH/GSH-px/SOD levels (K–N) *in vitro* model by si-AKAP1 + NDUFS1. $^{\#\#}p < 0.01$ compared with negative control group or si-negative control group; $^{**}p < 0.01$ compared with AKAP1 group or si-AKAP1 group.

renal patients with AHF. AKAP1 might be one novel target for AHF treatment. It may have diagnostic and predictive value in patients with kidney disease and AHF.

Under hemodynamic stress such as hypertension, the compensatory heart exhibits hypertrophy of myocardial cells, leading to progressive programmed cell death and ultimately entering heart failure [27]. Therefore, how to effectively respond to this cell death can serve as a new approach for early intervention in heart failure. Ferroptosis is essentially induced by lipid peroxide accumulation under ferrous catalysis. The main feature of ferroptosis is intact cell membrane lipid peroxidation, leading to the deposition of lethal ROS [28]. Heart failure is a heart structural or functional disease that leads to impaired cardiac function, making the cardiac output unable to meet the body's needs, mainly manifested as systemic and pulmonary congestion and inadequate tissue perfusion [29]. Cardiomyopathy, diabetes, degenerative valve disease, rheumatic heart disease, *etc*., and heart failure can be divided into diastolic and systolic based on physiological function, but there are still many unknowns in the relationship between heart failure and ferroptosis [30,31]. Ferroptosis has been extensively studied in the fields of tumors and neurodegenerative diseases, but its relationship with cardiovascular disease has been rarely discussed [10]. This study showed that AKAP1 up-regulation reduced ROS-induced lipid peroxidation ferroptosis *in vitro* model. Wan *et al*. [32] showed that AKAP1 plays a key role in mitochondrial fission through endothelial apoptosis. These data instructed that *AKAP1* gene reduced ROS-induced lipid peroxidation ferroptosis by mitochondrial damage in model of cute heart failure. In this study, we not measured the alterations of ultra-structure of heart, which was one insufficient for this experiment.

When mitochondrial function is normal, ROS in the body is maintained in a balanced state, participating in the regulation of oxidation-reduction and the transmission of biological information [33]. When the body is in an oxidative stress state, NDUFS1 subunit inactivation leads to electron respiratory chain dysfunction and the production of a large amount of reactive oxygen species, which has a dual effect on the regulation of tumors, indicating that NDUFS1 inactivation has a dual effect on disease development [34]. Our study determined that AKAP1 induced NDUFS1 expression to increase GPX4 activity level by the Ubiquitination of NDUFS1. Qi *et al*. [13] showed that AKAP1 deficiency exacerbated diabetic cardiomyopathy through mitochondrial dysfunction by NDUFS1. So, AKAP1 promoted NDUFS1 activity through the inhibition of ubiquitination of NDUFS1.

Conclusions

In conclusion, this study demonstrates that AKAP1 reduced ROS-induced lipid peroxidation ferroptosis through the inhibition of ubiquitination of NDUFS by mitochondrial damage in model of renal patients with AHF. AKAP1 in AHF suggested a novel target for AHF treatment. Therefore, AKAP1 is a potential target for the treatment of AHF or various types of cardiovascular disease.

Availability of Data and Materials

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

Author Contributions

YF designed the experiments, performed the experiments, YF, JX and RH collected and analyzed the data, drafted manuscript. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work to take public responsibility for appropriate portions of the content and agreed to be accountable for all aspects of the work in ensuring that questions related to its accuracy or integrity.

Ethics Approval and Consent to Participate

All patients were informed and signed informed consent voluntarily. This study was approved by the ethics committee of The First People's Hospital of Yongkang (No. 20200506L161) and complied with the guidelines outlined in the declaration of Helsinki were followed. All procedures were performed in accordance with the Guidance Suggestions for the Care and Use of Laboratory experiments (No. 20210312M023), formulated by the Ministry of Science and Technology of China.

Acknowledgment

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Conflict of Interest

The author declares no conflict of interest.

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