**ARRIVE Checklist**

Item 1. Study design

The present study was a one-way, two-phase trial in which 80 mice received intraperitoneal injection of isoproterenol and normal saline in phase 1. Phase 2 took berberine and normal saline placebo. Isoproterenol is given daily at 3mg. Kg-1 for one week. Berberine was given 5mg. Kg-1 and 10mg. Kg-1 daily intragastrically for one week. The individual mouse was considered the experimental unit within the studies.（Methods, paragraph 2 Establishment of cardiac hypertrophy model）

Item 2. Sample size

Eighty rats (20 in each group) were injected intraperitoneally with normal saline (n=20) in the control group and isoproterenol (n=60) in the other three groups (A,B,C). In the second stage, the rats in group A (n=18) and group B (n=16) were gavaged with berberine at A dose of (A.5mg/kg; B.10mg/kg), the rats in group C were intragastrically given the same volume of normal saline. The calculation of sample size was based on the results of the pre-experiment, and the formula of sample size with paired design was used: N=2\*[(μα+μβ) \*S/X]2. Where S is the variance of the differences between pairs obtained from pre-experiment or experience. X is the mean difference when the expected difference is required to be achieved. At the same time, according to the regulations of experimental animal design, no less than 4 rats in each group is considered statistically significant. Finally, 20 rats in each group is considered acceptable. （Methods, paragraph 2 Establishment of cardiac hypertrophy model；Results, paragraph 1 Rat Model;paragraph 2 Parameters of conventional two-dimensional echocardiography）

Item 3. Inclusion and exclusion criteria

These animals were included in the study if they successfully underwent the modeling process for ISO-induced cardiac hypertrophy. Eighty SD rats were randomized to the study and 6 of them died during the modeling process. Therefore, a total of 74 rats were included in this study. After the first phase of the experiment, 5 rats in the ISO group and the control group were randomly killed, and a total of 49 rats in the ISO group were subsequently included in the berberine intervention experiment. After the end of the experiment, 5 rats in each group were randomly killed.（Results, paragraph 1 Rat Model）

Item 4. Randomisation

Eighty male Sprague-Dawley rats (body weight 286±7g) were selected from Chengdu Dasuo Experimental Animal Co., Ltd. (Chengdu, China) and randomly divided into four groups, with 20 rats in each group. After 1 week of adaptive feeding, the control rats were intraperitoneally injected with normal saline, and the other three groups of rats were intraperitoneally injected with isoproterenol (3mg/kg) to induce cardiac hypertrophy. Use the standard = RAND() function in Microsoft Excel to generate random numbers. The method of randomization is as follows. The rats were randomly assigned to a group by an experimenter and weighed. A total of 80 animals were divided into four different weight groups (20 animals in each group). These weight groups were then randomly assigned to the experimental and control groups by another experimenter.（Methods, paragraph 2 Establishment of cardiac hypertrophy model）

Item 5. Blinding

For each rat, three different investigators were shown as follows: The first investigator (LH) performed the modeling process according to the random grouping table. The researcher was the only person who knew the distribution of the modeling group. A second investigator (KT) was responsible for the berberine treatment process, while a third investigator (YL) performed the anesthesia and surgical procedure. Finally, a fourth investigator(SY)(also unaware of the treatment) performed the echocardiography.

Item 6. Outcome measures

We evaluated the following parameters: left ventricular end-diastolic diameter (LVEDD), left ventricular end-systolic diameter (LVESD), end-diastolic interval thickness (IVS), left ventricular posterior wall thickness (LVPWD), left ventricular ejection fraction (LVEF) and shortened fraction (FS), heart rate (HR). , relative wall thickness (RWT), left ventricular mass index (LVMI), endocardial circumferential strain (CS), medial circumferential strain and epicardial circumferential strain, and pathological examination were used to determine the total tissue area of myocardial fibrosis. （Methods, paragraph 3 Echocardiography; paragraph 4 Layered Speckle Tracking echocardiography; paragraph 5 Histopathological analysis）

Item 7. Statistical methods

The continuous variable of a normal distribution was expressed as mean ± standard deviation. Non-normally distributed variables were expressed as the median. Kolmogorov-Smirnov test was used to verify that the continuous variable was normally distributed. Homogeneity of variance was evaluated by Levene’s test. The two groups of data were tested by a T test of independent samples. Paired T test was used to compare the data before and after . If the data for continuous variables satisfied normal distribution and homogeneity of variance, one-way ANOVA model was used, and the comparison among groups were performed with LSD method；Otherwise, the Kruskal-Wallis test was performed to compare the differences of the non-conforming measurement data. The correlation between GCS, Endo and other strain values and the percentage of myocardial collagen fiber deposition was analyzed by Pearson or Spearman correlation coefficient, and Spearman correlation coefficient was calculated.All statistical analyses were performed on SPSS 25.0 for Mac and all statistical tests were double-sided. P value <0.05 was considered statistically significant.（Methods, paragraph 6 Statistical analysis）

Item 8. Experimental animals

80 Male Sprague-Dawley rats [Grade II, Certificate No. SCXK (Chuan) 2020-030], weighing 286±7g, were purchased from Chengdu Dasuo Experimental Animal Co., Ltd. (Chengdu, China).（Methods, paragraph 1 Animals）

Item 9. Experimental procedures

 80 Male Sprague-Dawley rats were kept at the Medical Animal Center of the Sichuan Provincial People's Hospital. Rats were reared in a specific pathogen-free environment. The temperature of the feeding room was maintained at about 25℃ and the relative humidity was 60%. Automatically set 12-hour alternating light and dark environment. Rats were routinely fed and drank unlimited amounts of water. All experiments on rats were conducted in strict accordance with international ethical guidelines and National Institutes of Health guidelines for the use and care of laboratory animals. Eighty rats were randomly divided into four groups, with 20 rats in each group. After 1 week of adaptive feeding, the control rats were intraperitoneally injected with normal saline, and the other three groups of rats were intraperitoneally injected with isoproterenol (3mg/kg) to induce cardiac hypertrophy. After 7 days of continuous administration, the rats in the three groups after successful modeling were: berberine-treated group A, berberine-treated group B, and normal saline group C. Groups A and B were given berberine hydrochloride by intragastric gavage (groupA:5mg/kg;GroupB:10mg/kg), and group C was intragastrically given the same amount of normal saline. Gastric administration continued for 7 days.（Methods, paragraph 1 Animals; paragraph 2 Establishment of cardiac hypertrophy model）

Item 10. Results

Before modeling, after modeling, after intervention; After modeling, compared with the control group, IVS, LVPW, LVMI and RWT in the ISO group were significantly increased, with statistical significance (4.56 vs. 2.18; 2.85 and 2.01; 2.93 vs. 1.99; 1.11 vs. 0.78; P < 0.05). There were no significant changes in IVS, LVPW and RWT among groups A, B and C after gavage intervention (P>0.05). However, RWT decreased in all groups before and after self-control, but the difference was not statistically significant.

After modeling, the overall circumferential strain was reduced in the ISO group compared with the control group (GCS, −20.46% vs.−15.71%; P < 0.001). Compared with the control group, CS in endocardial and mid-wall layers decreased in the ISO group (− 29.57%-19.39% vs.− 20.11%-15.35%; P < 0.001). At the same time, after modeling, CS in endocardial layer and middle parietal layer at papillary muscle level of left ventricular short axis in the ISO group was significantly lower than before modeling, with statistical significance (P <0.05).

Before berberine treatment, there was no significant difference in the circular strain parameters of the papillary muscle level of the left ventricular short axis in normal saline group C, berberine group A (5mg/kg) and berberine group B (10mg/kg) (−16.12% vs.−15.68% vs.−15.85%; After berberine treatment, endocardial CS levels of left ventricular short axis papillary muscle in berberine A group (5mg/kg) and berberine B group (10mg/kg) were both higher than those in C group (−24.49% vs.−26.87% vs.−20.09%; P < 0.001; Berberine group B was more obvious (−24.49% vs.−26.87%; P < 0.001) . In the berberine treatment group, the model group and the control group, the horizontal and circular delamination strains of the papillary muscle of the left ventricular short axis showed gradient characteristics :Endo >, MID > and EPI, respectively.

Compared with control rats (1.05±0.05%, P <0.001), fibrosis was significantly increased in the ISO group rats (27.74±2.98%) after 7 days. After 7 days of berberine intragastric intervention, the fibrosis deposition of rats in groups A and B decreased (24.87±0.33%, P < 0.05) compared with that in group C without intervention. (23.29±0.40% vs 27.74±2.98%, P <0.01), group B was more obvious. Spearman rank correlation analysis was used to analyze the relationship between the stratified strain value and the percentage of myocardial interstitial fiber deposition (Q%). The results showed that Endo was positively correlated with the rate of myocardial interstitial fiber deposition (r=0.916, P <0.05), and GCS was positively correlated with the rate of myocardial interstitial fiber deposition (r=0.837,P <0.05).( Results, paragraph2-4)