https://doi.org/10.31925/farmacia.2023.4.20 **ORIGINAL ARTICLE**

PROTECTIVE EFFECTS OF ULTRASOUND-BASED PREOPERATIVE EXOGENOUS SACUBITRIL/VALSARTAN ON THE HEART AND KIDNEY OF PATIENTS UNDERGOING PERCUTANEOUS CORONARY INTERVENTION

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Abstract

This research aimed to demonstrate the protective effects of exogenous sacubitril/valsartan on the heart and kidney of patients undergoing percutaneous coronary intervention (PCI) preoperatively based on ultrasound. Three hundred patients undergoing PCI in our hospital were assigned to a control (Ctrl) group (150 patients receiving valsartan preoperatively) and a research (Res) group (150 patients receiving sacubitril/valsartan preoperatively). The myocardial injury, cardiac function (CF), renal function (RF) and complications of the two groups were compared preoperatively and postoperatively. The results showed that the troponin I (cTnI) and creatine kinase isoenzyme myocardial bands (CK-MB) in the two groups showed a decreasing trend postoperatively, and that of the Res group was more significant ($p < 0.05$). Postoperatively, the left ventricular end-diastolic volume (LVEDV) and left ventricular end-systolic volume (LVESV) of the two groups of patients decreased, being more significant in the Res group ($p < 0.05$). Postoperatively, blood urea nitrogen (BUN) and creatinine (Cr) in the two groups were decreased, the trend being more evident in the Res group ($p < 0.05$). The drug efficiency in the Ctrl group and Res group was 84.67% and 93.33%, respectively, and the effective rate of drugs in the Res group was y higher ($p < 0.05$). In summary, ultrasonography had a positive adoption value in evaluating the treatment effect of coronary intervention, and exogenous sacubitril/valsartan had an important protective effect on the heart and kidneys of patients undergoing PCI.

Rezumat

În cadrul acestui studiu au fost investigate efectele protectoare exogene ale sacubitril/valsartan asupra inimii și rinichilor la pacienții supuși intervenției coronariene percutanate (ICP), preoperator, pe baza ecografiei. Un număr de trei sute de pacienți supuși ICP au fost repartizați astfel: un grup de control (Ctrl) (150 de pacienți care au primit valsartan preoperator) și un grup de cercetare (Res) (150 de pacienți care au primit sacubitril/valsartan preoperator). Leziunea miocardică, funcția cardiacă (FC), funcția renală (RF) și complicațiile celor două grupuri au fost comparate preoperator și postoperator. Rezultatele au arătat că benzile miocardice ale troponinei I și ale izoenzimei creatin kinaza în cele două loturi au prezentat o tendință de scădere postoperator, cea din grupul Res fiind mai semnificativă ($p < 0,05$). Postoperator, volumele telediastolic și telesistolic ale ventriculului stâng din cele două loturi de pacienți au scăzut, fiind mai semnificative în grupul Res ($p < 0,05$). Postoperator, porțiunea azotată a ureei din sânge și creatinina au fost scăzute în cele două loturi, tendința fiind mai evidentă în grupul Res ($p < 0,05$). Eficiența medicamentelor în grupul Ctrl și grupul Res a fost de 84,67%, respectiv 93,33%. În concluzie, în urma evaluării prin ultrasonografie, asocierea sacubitril/valsartan a dovedit o protecție importantă asupra inimii și rinichilor la pacienții care au suferit IPC.

Keywords: ultrasound examination, exogenous sacubitril/valsartan, percutaneous coronary intervention, heart function, renal function, myocardial injury

Introduction

Myocardial infarction (MI) is common in middle-aged and elderly people and seriously plagues the normal life of patients [1]. Acute myocardial infarction (AMI) is a cardiovascular disease with rapid onset, great harm and high mortality [2]. The incidence of MI in men is superior to that in women. The mechanism of MI is vascular occlusion caused by atherosclerosis and blood flow is blocked, thus resulting in MI and seriously affecting heart function [3, 4]. When MI occurs, patients' action is blocked, the symptoms are obvious, the pain is strong and the risk is extremely high, so timely rescue is needed [5]. Thrombolysis and interventional surgery are the main means to alleviate the disease [6]. Vascular occlusion occurs in patients with MI, and intervention surgery is needed to dredge the blood vessels to restore blood supply and relieve the symptoms of cardiac

ischemia and hypoxia [7]. Interventional surgery has the advantages of rapid treatment, obvious curative effects, convenient operation, high safety and high recognition among patients [8].

Currently, the methods for the examination of cardiac function (CF) and structure mainly include imaging examination and coronary angiography [9]. In recent years, ultrasonic examination has become a common examination method for CF in clinical practice. This method has a good disease diagnosis effect, is non-invasive and simple, has a high resolution, and makes the cardiac structure and blood vessels clearer and more intuitive. It can markedly improve the diagnostic accuracy of patients and has been widely recognized in clinical practice [10, 11]. Most patients with AMI need coronary intervention, and intervention treatment will cause a certain degree of damage to vascular endothelial cells and adverse effects on the tissue cells of patients, causing myocardial necrosis of patients and even heart failure, which has an adverse effect on the prognosis of coronary intervention. Thus, drugs need to be taken to protect the vascular endothelium and alleviate the disease [12-14]. Sacubitril/valsartan can greatly inhibit ventricular remodelling and has high adoption value. It can delay the severity of AMI in patients and prevent the occurrence of heart failure and has been widely applied in clinical practice [15-17]. The cardiac and renal protective effects of ultrasound-based preoperative adoption of exogenous sacubitril/valsartan in patients who received percutaneous coronary intervention (PCI) were investigated. The myocardial injury, CF and renal function (RF) of patients taking valsartan and patients taking sacubitril/valsartan were analysed preoperatively and postoperatively, and the treatment efficiency of patients under different drug use was explored to provide clinical guidance to treat patients with AMI undergoing PCI.

Materials and Methods

Patients

A total of 300 patients with AMI undergoing PCI admitted to the Cangzhou Central Hospital, Cangzhou, China from June 2019 to December 2021 were recruited. Based on ultrasound examination, the protective effect of preoperative drug use on the heart and kidney of patients undergoing PCI was studied. This research was approved by the Ethics Committee of Cangzhou Central Hospital, Cangzhou, China and the patients and their families signed the informed consent form.

Inclusion criteria: (1) the patient's surgical and clinical medical records were complete; (2) patients having no other blood diseases; (3) patients with no contra-indications of ultrasonography and coronary angiography; (4) patients with clear consciousness and a high degree of cooperation; (5) patients and their families who signed the informed consent.

Exclusion criteria: (1) patients complicated with diseases of other vital organs; (2) patients with other malignant tumours; (3) patients with genetic diseases; (4) patients with communication difficulties; (5) pregnant or parturient women; (6) patients who were unwilling to participate in this study.

Grouping

Three hundred patients undergoing PCI for AMI were assigned to a control (Ctrl) group (150 patients receiving valsartan preoperatively) and a research (Res) group (150 patients receiving sacubitril/valsartan pre-operatively) randomly. The length of education of patients in the Ctrl group was 12.31 ± 1.62 years, while that of the Res group was 12.47 ± 1.77 years. The average age of patients in the Ctrl group was 52.45 ± 8.28 years old, and that in the Res group was 52.23 ± 8.86 years old. The body mass index (BMI) of patients in the Ctrl group was 22.47 ± 2.16 kg/m^2 and that of patients in the Res group was 22.16 ± 2.15 kg/m^2. There were 82 males and 68 females in the Ctrl group and 85 males and 65 females in the Res group. There was no marked difference in the years of education, average age, body mass index (BMI) and gender between the patients in the Ctrl group and Res group ($p > 0.05$), which was comparable. All the 300 patients with AMI were examined by ultrasound before and after PCI. Before the operation, patients in the Ctrl group took valsartan (Huahai Pharmaceutical Co., Ltd., China), 80 mg/time, once a day, and patients in the Res group took sacubitril/valsartan (Novartis Pharmaceutical Co., Ltd., Switzerland), 100 mg/time, twice a day. The CF, RF and complications of patients taking different drugs preoperatively and postoperatively were analysed.

Examination

All patients were examined for myocardial injury preoperatively and postoperatively. Venous blood samples were collected to detect serum Cardiac Troponin-I (cTnI) and creatine kinase isoenzyme myocardial band (CK-MB) levels. The inspection method was a chemiluminescence assay using the respective kits from Roche Diagnostics, Penzberg, Germany.

All patients were examined by ultrasound before and after surgery, and a colour Doppler ultrasound diagnostic instrument (DW-3101B, Xuzhou Dawei Electronic Equipment Co., Ltd., China) was employed for examination. The probes were S5-1 and S8-3, and the frequencies were 1-5 MHz and 3 - 8 MHz, respectively. The patient was placed in the left decubitus position, and the synchronous lead electrocardiogram was connected to measure the left ventricular end-diastolic volume (LVEDV) and left ventricular end-systolic volume (LVESV) of the patient.

RF tests were performed on all patients before and after surgery. Venous blood samples were extracted and centrifuged at 3,250 r/min for 19 min, and the supernatant was extracted to determine serum creatinine (Cr) and urea nitrogen (BUN) levels using a BS-380

biochemistry analyser (Mindray Medical Electronics Co., Ltd., China).

Observation indexes

Statistics were made for comparison of general data in the Ctrl group and those in the Res group, including gender, average age and BMI of patients in each group. The calculation method of BMI is shown in Eq. (1).

$$BMI = \frac{Weight}{Height^2}, \quad (1)$$

The echocardiography and coronary angiography of patients with AMI in the Ctrl group and Res group were analysed.

A comparison of myocardial injury between the Ctrl group and the Res group was performed. The main indicators were CK-MB and cTnI.

The CFs of the patients in the Ctrl group and the patients in the Res group were compared. The main indicators included left atrial diameter (LAD), LVEDV and LVESV.

The RF of patients in the Ctrl group and Res group was compared. The main indicators included Cr and BUN.

The treatment-effective rates of the patients in the Ctrl group and the patients in the Res group were compared. Significantly effective was no impairment of heart and RF. Effective is that the clinical symptoms of cardiovascular disease were relieved, and there was mild impairment of the heart and RF. Clinical symptoms of cardiovascular disease that were not relieved or worsened and severe damage to the heart and RF were considered invalid. The calculation method of the treatment effective rate is shown in Eq. (2).

$$Efficiency = \frac{Significant\ effect+Valid}{Total\ number\ of\ people}, \quad (2)$$

Statistical analysis

Excel 2016 (Microsoft Corporation, Washington, USA) and SPSS 20.0 (IBM, New York, USA) were employed. Mean ± standard deviation represented measurement data, which were tested by a *t*-test. Percentage (%) was how count data were denoted, which were tested by the χ^2 test. A value of $p < 0.05$ was considered statistically significant.

Results and Discussion

Analysis of colour echocardiography and coronary angiography in patients with AMI

Figure 1 illustrates the analysis of echocardiography and coronary angiography in a patient with AMI. A thrombus occurred in the left ventricular apex of the heart. Diffuse stenosis was observed in the middle to the distal segment of the RCA in the patient. Coronary angiography showed TIMI grade 2 flow in the distal part of the RCA.

Figure 1.

Analysis of colour echocardiography and coronary angiography in patients with AMI

A: colour echocardiography, B: coronary angiography. Patient 1 was a 56-year-old male with AMI

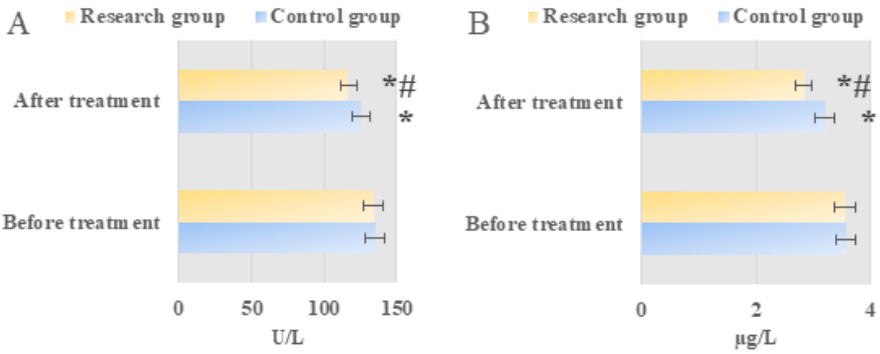

Figure 2.

Comparison of CK-MB and cTnI levels between patients in the Ctrl group and those in the Res group

A: CK-MB, B: cTnI, *$p < 0.05$ *vs.* preoperatively, #$p < 0.05$ *vs.* Ctrl

Comparison of myocardial injury

Figure 2 illustrates the comparison of CK-MB levels between groups. Before treatment, CK-MB values in the Ctrl group were 135.6 U/L, and those in the Res group were 134.2 U/L. After treatment, CK-MB was 125.7 U/L in the Ctrl group and 117.3 U/L in the Res group. Hence, CK-MB was decreased in both groups postoperatively, and the decrease in the Res group was more prominent ($p < 0.05$). Before treatment, the cTnI values in the Ctrl group and Res group were 3.58 μg/L and 3.56 μg/L, respectively. After treatment, cTnI was 3.21 μg/L in the Ctrl group and 2.84 μg/L in the Res group. Hence, the cTnI of patients in both groups was decreased postoperatively, and the decrease in patients in the Res group was more marked ($p < 0.05$).

Comparison of cardiac function

Figure 3 illustrates the LAD of patients in the Ctrl group and patients in the Res group. Before treatment, the LAD of patients in the Ctrl group was 36.4 mm and that of patients in the Res group was 36.8 mm. LAD of patients in the Ctrl group was 37.2 mm post-operatively and that of patients in the Res group was 35.2 mm. Hence, the LAD of patients in the Ctrl group was increased postoperatively, and the LAD of patients in the Res group was decreased ($p < 0.05$).

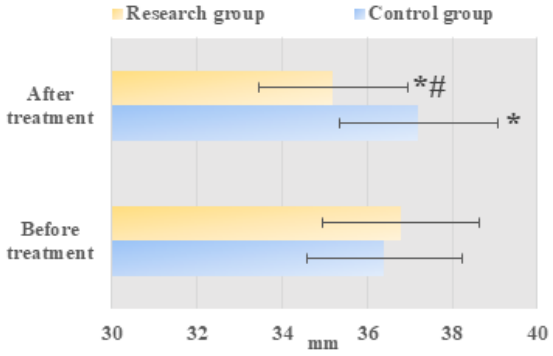

Figure 3.
Comparison of LAD conditions of patients in the Ctrl group and patients in the Res group
*$p < 0.05$ *vs.* preoperatively, #$p < 0.05$ *vs.* Ctrl

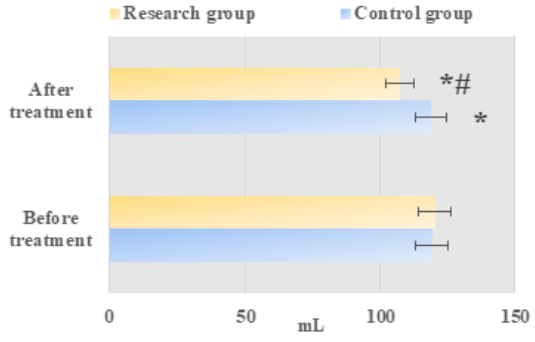

Figure 4.
Comparison of LVEDV conditions of patients in the Ctrl group and patients in the Res group
*p < 0.05 *vs.* preoperatively, #p < 0.05 *vs.* Ctrl

Figure 4 illustrates the LVEDV conditions of patients. Before treatment, the LVEDV of patients in the Ctrl group was 119.2 mL and that of patients in the Res group was 120.3 mL. Postoperatively, the LVEDV of patients in the Ctrl group was 118.9 mL and that of patients in the Res group was 107.3 mL. Post-operatively, LVEDV of patients in the two groups was decreased, and the decrease in patients in the Res group was more significant ($p < 0.05$).

Figure 5 illustrates the LVESV of patients in the Ctrl group and those in the Res group. Before treatment, the LVESV of patients in the Ctrl group was 55.3 mL and that of patients in the Res group was 56.4 mL. Postoperatively, LVESV was 51.2 mL in the Ctrl group and 48.3 mL in the Res group. Postoperatively, LVESV of both groups decreased, and the decrease in the Res group was more significant ($p < 0.05$).

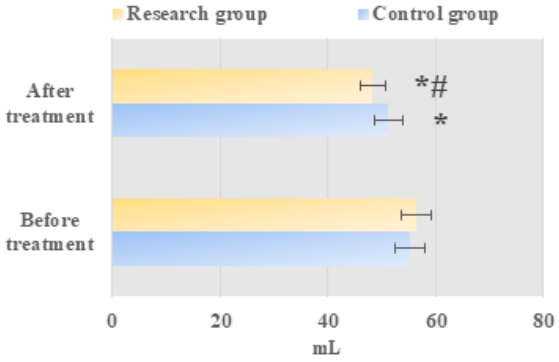

Figure 5.
Comparison of LVESV status of patients in Ctrl group and patients in Res group
*p < 0.05 *vs.* preoperatively, #p < 0.05 *vs.* Ctrl

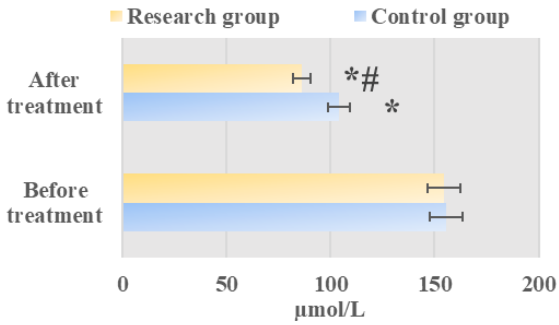

Figure 6.
Comparison of Cr levels of patients in the Ctrl group and patients in the Res group
*p < 0.05 *vs.* preoperatively, #p < 0.05 *vs.* Ctrl

Comparison of renal function

Figure 6 is a comparison of Cr levels between patients in the Ctrl group and patients in the Res group. Before treatment, Cr in patients in the Ctrl group was 155.6 μmol/L, while Cr in patients in the Res group was 154.6 μmol/L. After treatment, Cr in patients in the Ctrl group was 104.3 μmol/L and Cr in patients in the Res group was 86.3 μmol/L. Cr levels in patients in

both groups decreased postoperatively, and the decrease in patients in the Res group was more notable ($p < 0.05$).

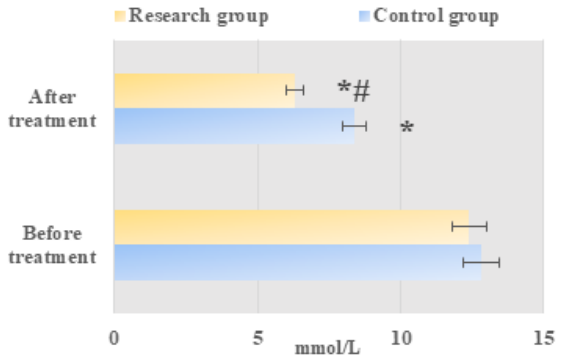

Figure 7.
Comparison of BUN levels of patients in the Ctrl group and patients in the Res group
*$p < 0.05$ *vs*. preoperatively, #$p < 0.05$ *vs*. Ctrl

Figure 7 illustrates the comparison of BUN levels between patients in the Ctrl group and those in the Res group. Before treatment, the BUN of patients in the Ctrl group was 12.8 mmol/L and that of patients in the Res group was 12.4 mmol/L. Postoperatively, the BUN of patients in the Ctrl group was 8.4 mmol/L and that of patients in the Res group was 6.3 mmol/L. Postoperatively, the BUN of patients in both groups was decreased, and the decrease in the Res group was more prominent ($p < 0.05$).

Comparison of treatment efficiency

Figure 8 illustrates the treatment effectiveness of the Ctrl group and Res group. In the Ctrl group, 89 patients showed obvious remission of cardiovascular disease, 38 patients showed effective remission of cardiovascular disease and 23 patients showed no remission or ineffective exacerbation of cardiovascular disease. The effective rate of drug treatment was 84.67%. In the Res group, 108 patients showed notable remission of cardiovascular disease, 32 patients showed effective remission of cardiovascular disease, 10 patients showed no remission or aggravation of cardiovascular disease and 10 patients showed no response. The effective rate was 93.33%. Hence, the treatment response rate was greatly higher in the Res group ($p < 0.05$).

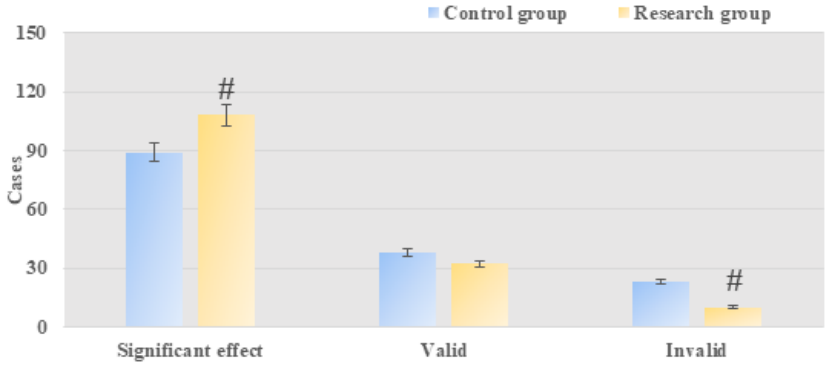

Figure 8.
Comparison of treatment effective rates of patients
#$p < 0.05$ *vs*. Ctrl

AMI has a high risk and a short rescue time, so it needs to dredge the blood vessels and restore the blood and oxygen supply function of the heart in a short time [18]. Interventional surgery is an effective means to treat AMI. Through interventional surgery, the blood supply to the heart can be quickly restored, the function of the heart can be improved, and the symptoms of patients can be relieved [19, 20]. Prevention and early diagnosis and treatment of diseases are of great importance, and drug treatment also has imperative value in AMI [21]. Different drugs control and relieve diseases through different action mechanisms, and it is of positive clinical value to explore the occurrence mechanism and protective effect of diseases [22]. A cardiac examination is of great value in understanding the condition and evaluating the treatment. Echocardiography is an imperative approach to assess the cardiac state and functional recovery of patients with AMI after interventional surgery, with the advantages of being a non-invasive, convenient operation and being able to directly see the results of the examination. It is widely utilized in cardiovascular diseases [23, 24]. Sacubitril/valsartan has unique advantages in the therapy of cardiovascular diseases in that it can inhibit the oxidative stress response, improve coagulation indicators and improve ventricular remodelling. It is highly safe, and it has high patient acceptance [25, 26]. Liu *et al*. [27] studied the clinical efficacy of sacubitril/valsartan sodium tablets (SVSTs) and found that they had high value in chronic heart failure (CHF). The efficacy and safety of SVST in the therapy of CHF were explored and the mortality, body weight change, urine volume, serum sodium change and incidence of unexpected adverse events in patients were analysed. SVST had good efficacy in the therapy of chronic heart failure and greatly reduced the mortality and complication incidence of patients. Ye *et al*. [28] evaluated the clinical efficacy and safety of sacubitril/valsartan in

the therapy of diabetic heart failure (HF) with medium ejection fraction after AMI (AMI) and found that the LVEDD of the Res group greatly decreased, with an amplitude greater than that of Ctrl group. The left ventricular ejection fraction of the Res group showed an increasing trend, with an amplitude greater than that of the Ctrl group. The readmission rate of the Res group was inferior to that of the Ctrl group. Sacubitril/valsartan had good adoption value for patients with diabetes and AMI accompanied by heart failure with medium ejection fraction. Zhang *et al*. [29] (2022) explored the early adoption of sacubitril/valsartan and found that it could inhibit ventricular remodelling after AMI, promote recovery from cardiovascular diseases, protect CF, reduce complications after MI, and help to prevent patient reoccurrence. This study analysed myocardial injury, CF and RF preoperatively and post-operatively in patients who had been pretreated with valsartan and sacubitril/valsartan based on ultrasound. The results showed that CK-MB and cTnI values in both groups tended to decrease postoperatively, and the trend in the Res group was greater ($p < 0.05$). Postoperatively, the Lad of patients in the Ctrl group tended to increase, while the Lad of patients in the Res group tended to decrease ($p < 0.05$). Postoperatively, LVEDV, LVESV, Cr levels and BUN levels of the two groups showed a decreasing trend, the effect being more evident in the Res group ($p < 0.05$). Hence, the preoperative use of sacubitril/valsartan drugs can prevent myocardial damage in patients, protect the patient's heart and renal function, and have good clinical effects. The therapeutic effects of valsartan and sacubitril/valsartan in patients were analysed. In the Ctrl group, 89 patients showed remarkable effects, 38 patients showed effective effects, 23 patients showed ineffective effects, and the efficiency of drug therapy was 84.67%. In the Res group, 108 patients showed remarkable effects, 32 patients showed effective effects, 10 patients showed ineffective effects, and the efficiency of drug treatment was 93.33%. The effective rate of drug treatment in the Res group was greatly higher than that in the Ctrl group ($p < 0.05$). Hence, the use of sacubitril/valsartan drugs can improve the therapy effect, enhance the safety of treatment, and has a positive adoption value.

Conclusions

Ultrasound can well diagnose and evaluate the therapeutic effect of a coronary intervention for AMI and has a high value in clinical adoption. The use of sacubitril/valsartan drugs before interventional surgery can protect the heart and RF of patients, improve the treatment effect, and reduce heart and kidney damage, which has a positive significance and a positive guiding value for the therapy of patients' diseases and can be utilized in clinical practice with high guiding value. Nevertheless, the shortcoming is that there is small sample size, and further research and verification are needed.

Conflict of interest

The authors declare no conflict of interest.

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