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Original Article

Influence of renal sympathetic denervation on the cardiac function of dogs with heart failure

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Abstract: Objective: This study aimed to investigate the influence of renal sympathetic denervation (RSDN) on the cardiac function of dogs with heart failure. Methods: A total of 40 dogs were randomly assigned into RSDN group and control group (n=20 per group). In RSDN group, dogs received radiofrequency ablation of bilateral renal arteries; dogs in control group received femoral artery puncture alone. Pacemaker (VOO module) was implanted in 40 dogs, and rapid right ventricular pacing was introduced to establish heart failure model. The maximum left ventricular end systolic diameter (LVESD), maximum left ventricular end-diastolic diameter (LVEDD), cardiac output (CO), cardiac index (CI), left ventricular systolic pressure (LVSP), left ventricular diastolic pressure (LVDP), maximum systolic blood pressure rise rate (dp/dtmax), maximum diastolic blood pressure drop rate (-dp/dtmax), heart rate (HR), peripheral renin, norepinephrine, angiotensin II, aldosterone, glomerular filtration rate (GFR) and renal blood flow were measured. Statistical analysis was performed with SPSS version 17.0. Results: The peripheral renin, norepinephrine, angiotensin II, aldosterone, LVDP, LVESD and LVEDD in RSDN group were significantly lower than in control group, but the left ventricular ejection fraction, CI, CO, LVSP, dp/dtmax, and -dp/dtmax in RSDN group were markedly higher than in control group. Conclusion: In heart failure dogs, RSDN may inhibit the renal sympathetic activity and reduce systemic sympathetic activity, attenuate heart enlargement, mitigate reduced myocardial contractility, suppress the myocardial remodeling due to right ventricular pacing induced heart failure and improve the symptoms of heart failure and cardiac function.

Keywords: Heart failure, renal sympathetic denervation, dog, right ventricular pacing, sympathetic nervous system

Introduction

Heart failure is a clinical syndrome due to the structural or functional abnormality of the heart which may affect the cardiac perfusion or heart beat, and is also the end stage of heart diseases [1]. Heart failure is usually accompanied by extensive adrenergic nervous system excitation, parasympathetic nervous system inhibition, renin-angiotensin-aldosterone system (RAAS) activation, extensive vasoconstriction, and sodium and water retention. In the presence of heart failure, the density of β-adrenergic receptor reduces, myocardial contractility fails to increase, sodium and water retention and vasoconstriction further increase the cardiac preload and afterload and visceral injury, and the renal blood flow reduces, which deteriorates heart failure, resulting in a vicious cycle of disease progression [1].

RAAS is an important humoral regulation system in humans, and its excitation may promote the release of neurotransmitters from the adrenergic nerves, induce the contraction of systemic arterioles and veins leading to blood pressure increase, elevate the central sympathetic vasoconstrictor tone, facilitate the release of vasopressin and adrenocorticotropic hormone, increase the synthesis and secretion of aldosterone leading to sodium and water retention, inhibit the left ventricular systolic function and cause the myocardial remodeling. RASS may participate in the pathophysiology of different diseases including heart failure, hypertension, and arrhythmias by above mechanisms. Renal sympathetic nerve may activate RASS via the adrenergic nerves [1-3].

In 2009, Krum et al. for the first time used renal sympathetic denervation (RSDN) in the therapy

of refractory hypertension and confirmed the safety of renal sympathetic nerve ablation with simplicity catheter and its effectiveness in the therapy of refractory hypertension [4]. Recently, clinical trials reveal that RSDN may not only reduce the renal sympathetic activity, but inhibit the activities of other sympathetic nerves, and the heart volume and cardiac function are improved after RSDN in patients with refractory hypertension [5-7]. Animal experiments also indicate that RSDN may delay the progression of myocardial hypertrophy [8]. However, evidence on the therapy of heart failure with RSDN is still insufficient. In the present study, right ventricular pacing was introduced in adult dogs to establish the heart failure model, and radiofrequency ablation of bilateral renal arteries was employed for RSDN, aiming to investigate the influence of RSDN on the cardiac function of dogs with heart failure.

Materials and methods

Materials

A total of 40 crossbred canines aged 10-12 months and weighing 16.2-18.4 kg were purchased from the Experimental Animal Center of Shanghai Jiaotong University. Radiofrequency ablation device (STOCKERT EP SHUTTLE, Johnson & Johnson, USA), 6 F endocardial electrode catheter (Johnson & Johnson, USA), Medtronic pacemaker (Medtronic Company), HEM-8102A Omron Blood Pressure Monitor (Shenzhen Omron Corporation), Innova 3100 digital subtraction angiography (US General Electric Company), Philips iE33 Multifunction Ultrasound, S5-1 probe (frequency: 2-4 MHz; Philips, Netherlands), SAR-830A ventilator for small animals (CWE ,USA), pentobarbital sodium (Sigma, USA), penicillin (Hangzhou Minsheng Pharmaceutical Company), renin detection kit (Sigma, USA), epinephrine detection kit (Sigma, USA), norepinephrine detection kit (Sigma, USA) and aldosterone detection kit (Sigma, USA) were used in this study.

Radiofrequency ablation of the renal sympathetic nerves

A total of 40 dogs were randomly assigned into two groups: RSDN group and control group (n=20 per group), and animals were numbed at the ear. Before study, dogs received food and water were fasting for 10 h and then fastened to an operating table. After general anesthesia by intravenous 3% pentobarbital sodium at 30 mg/kg and skin preparation, additional 50 mg of pentobarbital sodium was intravenously injected according to the animals' response 30-60 min later. Then, endotracheal intubation and subsequent mechanical ventilation were conducted, followed by continuous monitoring of electrocardiogram. The right or left femoral artery was punctured, and a 6 F endocardial electrode catheter was implanted for radiofrequency ablation. In RSDN group, ablation electrode plate was implanted in the back, and ablation was performed at 50°C and at 6-8 W. A renal artery was ablated at 0.5 cm away from the first bifurcation for 60 s, the probed was slightly retracted, and the catheter was rotated. Then, the artery was ablated at 4-6 sites in a spiral manner with a distance of 0.5 cm between two adjacent sites. In control group, only femoral artery was punctured, and ablation was not conducted. After surgery, animals were intramuscularly injected with penicillin (800000 U) for 3 consecutive days for infection prophylaxis [9, 10].

Establishment of heart failure model

Pre-operative preparation and intravenous anesthesia were conducted according to abovementioned. The carotid pulse was palpable at 2 cm right away from the trachea, and right external jugular vein was punctured at 0.5 cm away from the carotid pulse site. Then, an electrode was implanted in the right ventricle. Under the X ray, the electrode was fixed in the trabecular muscles of right ventricular apex. The pacing threshold was 0.3-1.5 V, the height of R wave was 4-10 mV, and the impedance was 0.3-1.0 KΩ. The pacemaker was connected, and the pacing frequency was set at 230 beat/min (VOO module). A bag was prepared to fix the pacemaker, and washed with gentamicin (320000 U). Then, the wound was closed. After surgery, animals were intramuscularly injected with penicillin (800000 U) for 3 consecutive days for infection prophylaxis. In addition, the appetite, activity and respiration were monitored, the surface electrocardiogram was detected every week, the pacing rhythm was maintained stable, and pacing was done for 4 weeks [11, 12].

Cardiac echocardiography and measurement of hemodynamics

Cardiac echocardiography was performed before RSDN and pacemaker implantation and at

Table 1. Clinical parameters of dogs before and after pacing in both groups

Parameters	RSDN group		Control group	
	Before pacing	4 weeks after pacing	Before pacing	4 weeks after pacing
HR (beats/min)	140±19.21	165±15.61*,#	148±16.29	179±20.02*
RR (breaths/min)	19±2.95	24±3.89*,#	16±7.86	29±5.07*
CR (μmol/l)	46.35±9.25	43.97±10.35**,#	42.24±8.76	45.32±6.52**
BUN (mmol/l)	3.42±0.63	4.56±0.91**,#	3.86±0.89	3.97±0.68**
UA (μmol/l)	6.54±1.58	7.21±1.92**,#	7.20±2.01	7.35±1.24**
BNP (pg/ml)	32±4.62	99±20.01*,#	37±6.20	187±25.63*

Note: *P<0.05: before vs. after pacing; **P>0.05: before vs. after pacing; #P<0.05: RSDN vs control group after pacing.

4 weeks after pacemaker implantation, and the left ventricular end systolic diameter (LVESD), left ventricular end-diastolic diameter (LVEDD), cardiac output (CO), cardiac index (CI), and left ventricular ejection fraction (EF) were measured. In addition, before RSDN and at 4 weeks after pacemaker implantation, femoral artery was punctured again, and the left ventricular systolic pressure (LVSP), left ventricular diastolic pressure (LVDP), maximum systolic blood pressure rise rate (dp/dtmax), and maximum diastolic blood pressure drop rate (-dp/dtmax) were measured.

Monitoring of blood parameters and vital signs

Before RSDN and pacemaker implantation and at 4 weeks after pacemaker implantation, the blood pressure, heart rate (HR), and respiration rate (RR) were recorded. At the same time, venous blood (6 ml) was collected from the femoral vein and centrifuged at 2500 rpm for 10 min. The plasma was collected, and processed for the detection of rennin (R), epinephrine (E), norepinephrine (NE), angiotensin II (ATII), and aldosterone (AD) according to manufacturer's instructions.

Statistical analysis

Data were input into EXCEL and statistical analysis was performed with SPSS version 17.0. Quantitative data are expressed as mean ± standard deviation, and comparisons between two groups were done with t test. Parameters measured before and after surgery were compared with paired t test. A value of $P<0.05$ was considered statistically significant.

Results

Characteristics of dogs

Results showed there were no marked differences in the age, body weight, blood pressure, heart rate, respiration rate and kidney function between RSDN group and control group at baseline (P>0.05). After RSDN, the activities, appetite and vital signs remained unchanged. At 2 weeks after right ventricular pacing, dogs showed reduced activities and loss of appetite. At 4 weeks after right ventricular pacing, above symptoms deteriorated, shortness of breath was also present, moist rales were heard by auscultation, and HR and RR increased. The HR was 140±19.21 beats/min before surgery and 165±15.61 beats/min after surgery in RSDN group and was 148±16.29 beats/min before surgery and 179±20.02 beats/min after surgery in control group. The RR was 19±2.95 breaths/min before surgery and 24±3.89 breaths/min after surgery in RSDN group and was 16±7.86 breaths/min before surgery and 29±5.07 breaths/min after surgery in control group. BNP increased after surgery in both groups (RSDN group: 32±4.62 pg/ml vs. 99±20.01 pg/ml; control group: 37±6.20 pg/ml vs 187±25.63 pg/ml). Paired t test showed significant differences in above parameters before and after surgery. Moreover, marked differences were also noted between RSDN group and control group (P<0.05). However, the kidney function remained unchanged during the experiment (P>0.05) (**Table 1**).

Cardiac function and hemodynamics

Results showed the blood pressure, HR, LVEDS, LVEDD, LVEF, CO and CI at 4 weeks after radiofrequency ablation (before pacemaker implantation) were comparable to those before radiofrequency ablation (P>0.05) (**Table 2**). This implies that RSDN has no influence on the blood pressure, HR, cardiac volume and cardiac function of healthy dogs.

The SBP reduced after heart failure in both groups. SBP reduced from 132±16.42 mmHg

Table 2. Blood pressure, HR, cardiac volume and cardiac function before and after radiofrequency ablation in RSDN and control groups

Parameters	RSDN group			Control group		
	Before ablation	After ablation	P	Before false surgery	After false surgery	P
SBP (mmHg)	132±16.42	128±20.42	0.18	127±20.67	129±19.56	0.24
DBP (mmHg)	78±14.60	78±13.80	0.12	75±15.68	75±15.72	0.19
HR (beats/min)	140±18.34	140±19.21	0.27	142±19.79	148±16.29	0.18
LVEDS (mm)	10.8±3.24	10.9±2.27	0.32	10.8±2.23	10.2±2.31	0.33
LVEDD (mm)	29.7±4.02	29.6±3.04	0.59	27.9±5.68	28.9±3.25	0.5
LVEF (%)	63.6±9.23	67.6±9.23	0.68	67.4±9.28	66.7±10.20	0.21
CO (l/min)	3.94±0.65	3.92±0.69	0.62	3.94±0.72	3.91±0.70	0.42
CI (l/min·Kg)	0.25±0.07	0.23±0.06	0.55	0.27±0.08	0.26±0.08	0.53
Parameters	RSDN group			Control group		
	Before ablation	After ablation	P	Before false surgery	After false surgery	P
SBP (mmHg)	132±16.42	128±20.42	0.18*,#	127±20.67	129±19.56	0.24*
DBP (mmHg)	78±14.60	78±13.80	0.12*,#	75±15.68	75±15.72	0.19*
HR (beats/min)	140±18.34	140±19.21	0.27*,#	142±19.79	148±16.29	0.18*
LVEDS (mm)	10.8±3.24	10.9±2.27	0.32*,#	10.8±2.23	10.2±2.31	0.33*
LVEDD (mm)	29.7±4.02	29.6±3.04	0.59*,#	27.9±5.68	28.9±3.25	0.50*
LVEF (%)	63.6±9.23	67.6±9.23	0.68*,#	67.4±9.28	66.7±10.20	0.21*
CO (l/min)	3.94±0.65	3.92±0.69	0.62*,#	3.94±0.72	3.91±0.70	0.42*
CI (l/min·Kg)	0.25±0.07	0.23±0.06	0.55*,#	0.27±0.08	0.26±0.08	0.53*

Note: *P>0.05, before vs. after ablation in RSDN group, as well as before vs. after false surgery in control group; #P>0.05: RSDN group vs. control group after ablation or false surgery.

Table 3. Heart function and hemodynamics in RSDN group and control group

	RSDN group		Control group	
	Before pacing	4 weeks after pacing	Before pacing	4 weeks after pacing
SBP (mmHg)	132±16.42	122±10.43#	129±19.56	110±14.42
DBP (mmHg)	78±13.80	76±15.67#	75±15.72	80±16.04
LVEDS (mm)	10.9±2.27	13.2±2.27#	10.2±2.31	17.5±4.32
LVEDD (mm)	29.6±3.04	30.6±2.85#	28.9±3.25	36.4±8.34
LVEF (%)	63.6±9.23	43.89±6.88#	66.7±10.20	35.21±5.72
CO (l/min)	3.92±0.69	1.82±0.71#	3.91±0.70	1.42±0.46
CI (l/min.Kg)	0.29±0.06	0.12±0.06#	0.26±0.08	0.10±0.05
+dp/dtmax (mmHg/s)	4230.24±687.28	3874.01±523.86#	4248.36±665.21	2437±459.87
-dp/dtmax (mmHg/s)	3211.48±659.68	2645.24±670.35#	3225.42±652.58	1841.56±609.52
LVSP (mmHg)	133±17.26	125±14.32#	131±19.65	114±12.86
LVDP (mmHg)	3.23±1.80	2.99±2.76*,#	3.12±1.96	20.15±4.53

Note: *P<0.05 before pacing vs. 4 weeks after pacing; #P<0.05: RSDN vs. control group after pacing.

to 122±10.43 mmHg in RSDN group and from 129±19.56 mmHg to 110±14.42 mmHg in control group. In addition, the left ventricle was enlarged in both groups. LVEDS increased from 10.9±2.27 to 13.2±2.27 mm in RSDN group and from 10.2±2.3 to 17.5±4.32 mm in control group. The EF reduced from 63.6±9.23% to 43.89±6.88% in RSDN group and from 66.7±10.20% to 35.21±5.72% in control group. CO reduced from 3.92±0.69% to 1.82±0.71% in

Table 4. Sympathetic activities in RSDN group and control group before and after pacing

	RSDN group		Control group	
	Before pacing	4 weeks after pacing	Before pacing	4 weeks after pacing
E (ng/ml)	280.36±42.32	290.36±42.32*,#	279.97±45.24	362.69±42.54*
RNA (ng/ml)	212.35±32.80	230.04±32.80*,#	217.51±29.65	305.461±39.68*
AD (ng/ml)	226±34.25	246±48.37*,#	230±29.26	408±38.56*
ATII (pg/ml)	146±18.25	172±25.04*,#	152±26.54	280±48.08*
NE (ng/ml)	286.76±46.29	316.76±46.29*,#	279.65±39.89	425.65±50.54*

Note: *P<0.05 before pacing vs. 4 weeks after pacing; #P<0.05: RSDN vs control group after pacing.

RSDN group and from 3.91±0.70 to 1.42±0.46 in control group. The CI reduced from 0.29±0.06 to 0.12±0.06 in RSDN group and from 0.26± 0.08 to 0.10±0.05 in control group. Paired t test showed the heart function after heart failure was significantly different from that before heart failure. Moreover, the reductions in the SBP, LVEF, CO and CO of control group were significantly higher than those of RSDN group (P<0.05) and the pulse pressure in control group was markedly lower than in RSDN group (P<0.05) (**Table 3**).

+dp/dtmax reduced after heart failure in both groups. +dp/dtmax reduced from 4230.24± 687.28 mmHg/s to 3874.01±523.86 mmHg/s in RSDN group and from 4248.36±665.21 mmHg/s to 2437±459.87 mmHg/s in control group. +dp/dtmax in RSDN group was significantly higher than in control group (P<0.05). -dp/dtmax also reduced markedly after heart failure in both groups (P<0.05). -dp/dtmax reduced from 3211.48±659.68 mmHg/s to 2645.24±670.35 mmHg/s in RSDN group and from 3225.42±652.58 mmHg/s to 1841.56 ±609.52 mmHg/s in control group, and the reduction in RSDN group was significantly lower than in control group (P<0.05). LVSP reduced from 133±17.26 mmHg to 125±14.32 mmHg in RSDN group and from 131±19.65 mmHg to 114±12.86 mmHg, and LVSP in RSDN group was significantly higher than in control group. The LVDP remained unchanged in RSDN group (P>0.05) (3.23±1.80 mmHg vs. 2.99± 2.76 mmHg), but LVDP in control group increased significantly (3.12±1.96 mmHg vs. 20.15± 4.53 mmHg). After heart failure, LVDP in RSDN group was significantly lower than in control group (P<0.05) (**Table 3**).

Sympathetic activities in RSDN group and control group

At 4 weeks after right ventricular pacing, the peripheral R, E, NE, AD and ATII increased significantly, and these parameters in RSDN group were markedly lower than in control group (P<0.05). The R increased from 280.36±42.32 ng/ml to 290.36±42.32 ng/ml in RSDN group and from 279.97±45.24 ng/ml to 362.69±42.54 ng/ml in control group. The E increased from 212.35±32.80 ng/ml to 230.04±32.80 ng/ml in RSDN group and from 217.51±29.65 ng/ml to 305.461±39.68 ng/ml in control group. AD increased from 226±34.25 ng/ml to 246± 48.37 in RSDN group and from 230±29.26 ng/ml to 408±38.56 ng/ml in control group. ATII increased from 146±18.25 ng/ml to 172± 25.04 ng/ml in RSDN group and from 152± 26.54 pg/ml to 280±48.08 pg/ml in control group. The NE increased from 286.76±46.29 ng/ml to 316.76±46.29 ng/ml in RSDN group and from 279.65±39.89 ng/ml to 425.65± 50.54 ng/ml in control group (**Table 4**).

Discussion

Renal sympathetic nerves include afferent and efferent ones. The fiber endings of afferent nerves are mainly distributed in the proximal ureter, pelvis and regions around the major vessels of the kidney. In addition, there are also sympathetic nerves in the glomeruli, proximal and distal convoluted tubules and renal medulla. The cell body of afferent nerves localizes in the dorsal root ganglion at T6-L4 and projects to several regions in the central nervous system to regulate the efferent signals. The central regulatory region of efferent nerves localizes at the head of ventrolateral medulla, and the axons of efferent nerves cross the T10-L3 sympathetic trunk to celiac ganglion, superior mesenteric ganglion and aorticorenal ganglion where the neurons are replaced with other neurons. Postganglionic fibers wrap the renal artery and are distributed in small vessel, renal cortex, juxtamedullary glomerulus and renal tubules along the renal artery. The renal sympa-

thetic nerve excitation may stimulate the juxtaglomerular cells to secret renin, leading to the increased RASS activity. Renin acts on the renal vascular smooth muscle to induce the contraction of renal vessels, which reduces renal blood flow and glomerular filtration rate and increases sodium and water retention. The renal sympathetic nerve may also activate the sympathetic center to increase the systemic sympathetic activity [13]. In addition, renin acts on β receptor to increase the myocardial contractility and heart rate and promote myocardial hypertrophy, which may compensate the heart failure at early stage, but finally cause the deterioration of myocardial remodeling and reduce the β receptor density, leading to decompensation and deterioration of heart failure.

Studies have shown that long lasting excessive sympathetic excitation may promote the myocardial remodeling and deteriorate cardiac function, and to inhibit the RASS is able to suppress the myocardial remodeling during heart failure [14]. Investigators reveal that renal sympathetic activity increases significantly in mice with heart failure [15]. During the heart failure, renal sympathetic nerves are preferentially activated, and renal norepinephrine is an important prognostic factor of all-cause mortality in heart failure [16]. During heart failure, the sensitivity of aortic and carotid baroreflex reduces, but the central sympathetic efferent and renal sympathetic activities increase, and the activity of pulmonary stretch receptors reduces, which compromises the regulation of renal sympathetic activity. The integration and processing of afferent signals in the central nervous system may elevate the sympathetic efferent activity, especially the renal sympathetic activity. After renal sympathetic excitation, postganglionic nerve fibers may release norepinephrine which acts on juxtaglomerular cells to promote renin secretion and further increase ATII. Moreover, ATII may further increase the sympathetic activity, leading to a pathological positive feedback during heart failure. Thus, to block the renal sympathetic nerves may suppress their regulatory effect on the kidney and inhibit this feedback.

Ablation of the renal sympathetic nerves is a new technique used for renal denervation. On the basis of anatomical distribution of renal sympathetic nerves along the renal artery, femoral artery puncture is conducted, and ablation catheter is inserted to the distal end of renal artery. The radiofrequency energy acts on the vascular endothelial cells, then the catheter is withdrawn and rotated for further ablation, leading to ablation at different sites to disrupt the renal sympathetic network. This technique has favorable safety and few complications. It was first used in the therapy of refractory hypertension and its safety and effectiveness have been preliminarily confirmed in studies [17]. Recent studies reveal that heart failure patients may benefit from the ablation of renal sympathetic nerves [6]. In the study of Nozawa et al., ablation of bilateral renal arteries was conducted in rats, and then coronary artery was ligated 2 days later to establish acute myocardial infarction model. They found that RSDN could significantly improve the sodium and water retention and the left ventricular filling pressure as well as the heart failure of rats with myocardial infarction [18]. Schirmer et al. investigated the therapeutic effect of RSDN on refractory hypertension, and found that RSDN could reduce the left ventricular mass and improve the diastolic function, which were independent of blood pressure change [19]. In 2012, investigators also revealed that RSDN could significantly reduce the sympathetic activity and RAAS activity of rats with myocardial infarction and markedly improve the heart failure, and reverse the myocardial remodeling and sodium and water retention after myocardial infarction [20]. In a study, 7 patients with NYHA class III-IV (heart failure) were investigated, and results indicated that the activity tolerance, cardiac function and symptoms of heart failure were significantly improved in patients at 6 months after RSDN [21].

In the present study, right apex pacing was introduced to establish heart failure model in dogs and the influence of renal sympathetic radiofrequency ablation on the heart failure was investigated. Our results showed the renal blood flow and kidney function remained unchanged after radiofrequency ablation of the renal sympathetic nerves. The blood pressure, heart rate, LVESD, LVEDD, CO, CI, left ventricular EF, LVSP and LVDP remained unchanged, suggesting that radiofrequency ablation of the renal sympathetic nerves has no influence on the renal blood flow and kidney function as well as the heart volume and cardiac function. In addition, after introduction of heart failure,

dogs developed symptoms (such as loss of appetite, reduced activities) and signs (pulmonary rales, increased heart rate, increased respiration rate) of heart failure. However, in dogs with radiofrequency ablation, the symptoms were improved to a certain extent, the heart rate and respiration rate reduced as compared to control group, and pulmonary rales were also less heard. Heart ultrasonography showed the LVESD and LVEDD increased in both groups and the left ventricular EF, CO and CI reduced in both groups after introduction of heart failure. However, the increases in LVESD and LVEDD in control group were higher than in RSDN group, and the reductions in left ventricular EF, CO and CI in control group were more obvious as compared to RSDN group. After introduction of heart failure, the hemodynamics changed significantly: LVSP, dp/dtmax and -dp/dtmax reduced significantly, and LVDP increased markedly, but the changes in these parameters were more obvious in control group. In addition, we further detected the biochemical parameters related to sympathetic excitation, and results showed the R, E, NE, AD and ATII increased in both group after heart failure, but the increases in control group were higher than in RSDN group. This indicates that RSDN inhibits the renal sympathetic activity, reduces NE, R, AT and AD, inhibits the RAAS activation and reduces systemic sympathetic activity. In addition, RSDN also suppresses the heart enlargement, compromises the reduced myocardial contractility and inhibit the myocardial remodeling due right ventricular pacing induced heart failure, leading to the improvement of symptoms of heart failure and cardiac function.

RSDN exerts therapeutic effect on the heart failure, but the specific mechanism is still poorly understood. In addition, results about its therapeutic effect are mainly from experiments in animals, and few studies have been conducted to investigate the efficacy of RSDN in the therapy of heart failure patients. Thus, more multicenter studies with large sample size are required to confirm our findings, standardize the inclusion criteria for RSDN therapy and explore the role of RSDN in the therapy of heart failure [22].

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Disclosure of conflict of interest

None.

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