**Effects of Intravenous Atrial Natriuretic Peptide on Cardiac Sympathetic Nerve Activity and Left Ventricular Remodeling in Patients With First Anterior Acute Myocardial Infarction**

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**Objectives**

We sought to evaluate the effects of atrial natriuretic peptide (ANP) on cardiac sympathetic nerve activity (CSNA) and left ventricular (LV) remodeling in patients with first anterior acute myocardial infarction (AMI) after primary coronary angioplasty.

**Background**

The activation of the renin-angiotensin-aldosterone system (RAAS) prevents the uptake of norepinephrine in the myocardium. Atrial natriuretic peptide, a circulating hormone of cardiac origin, has vasodilatory and diuretic properties, and can inhibit the RAAS.

**Methods**

We studied 50 patients with first anterior AMI who were randomly assigned to receive ANP (group A) or isosorbide dinitrate (group B) before and after primary coronary angioplasty. The ANP or ISDN was continuously infused for 48 h. The extent score (ES) was determined from 99mTc-pyrophosphate scintigraphy to evaluate the area of initial myocardial damage 3 to 5 days after primary angioplasty. The LV end-diastolic volume (LVEDV) and LV ejection fraction (LVEF) were determined by left ventriculography 2 weeks later. The delayed heart/mediastinum count (H/M) ratio, delayed total defect score (TDS), and washout rate (WR) were determined from 123I-metaiodobenzylguanidine scintigraphy after 3 weeks.

**Results**

After primary angioplasty, age, gender, risk factors, peak serum creatine phosphokinase concentration, recanalization time, and ES were similar in the 2 groups. However, in group A (n = 25), the TDS was significantly lower (34 ± 8 vs. 41 ± 8; p < 0.05), the H/M ratio was significantly higher (1.96 ± 0.18 vs. 1.74 ± 0.23; p < 0.05), and the WR was significantly lower (35 ± 8% vs. 44 ± 12%; p < 0.005) than in group B (n = 25). Moreover, the LVEDV and LVEF in group A were better than in group B (LVEDV: 85.5 ± 28.5 ml vs. 106.3 ± 39.4 ml [p < 0.05]; LVEF: 47.9 ± 10.2% vs. 41.5 ± 11.8% [p < 0.05]).

**Conclusions**

Intravenous ANP improves CSNA and prevents LV remodeling in patients with first anterior AMI. *(J Am Coll Cardiol 2007;49:667–74) © 2007 by the American College of Cardiology Foundation*

Event-free survival after acute myocardial infarction (AMI) is influenced by the extent of residual myocardial ischemia (1) and the global left ventricular (LV) ejection fraction (LVEF) (2). Patients with LV dysfunction are more likely to have progressive LV dilation, which is an independent determinant of long-term survival (3). Moreover, activation of the sympathetic nervous system is one of the cardinal pathophysiologic abnormalities associated with the failing human heart (4). Therefore, plasma norepinephrine concentrations affect the morbidity and mortality in patients with AMI (5).

In the acute phase of AMI, nitroglycerin has been reported to have a favorable effect in preventing LV remodeling (6). However, this agent may stimulate the renin-angiotensin-aldosterone system (RAAS) despite its beneficial hemodynamic effect (7). In contrast, atrial natriuretic peptide (ANP) has a wide range of potent biologic effects, including natriuretic, diuretic, and vasodilatory properties and inhibition of the RAAS (8). The efficacy of intravenous administration of ANP in patients with acute myocardial...
infarction has been reported previously (9). In that report, the intravenous administration of ANP prevented LV dilation and remodeling after primary coronary angioplasty in patients with AMI.

Myocardial imaging with $^{123}$I-MIBG, an analog of norepinephrine, is useful for detecting abnormalities in the myocardial adrenergic nervous system in patients with AMI (10). Myocardial ischemic area and cardiac $^{123}$I-MIBG defect size are correlated in patients undergoing reperfusion therapy for acute coronary syndromes (11). Many reports have suggested that inhibition of the RAAS can improve cardiac sympathetic nerve activity, based on cardiac $^{123}$I-MIBG scintigraphic studies, in patients with heart disease (12–20). However, no reports discuss the changes in cardiac $^{123}$I-MIBG scintigraphic findings in response to ANP administration in patients with AMI, although we previously reported improved cardiac sympathetic nerve activity (CSNA) in patients with nonischemic decompensated acute heart failure (17).

**Methods**

**Patients.** From April 2003 through February 2006, 66 patients who were admitted to the Coronary Care Unit (CCU) of our institution for their first myocardial infarction of the anterior wall and showed Thrombolysis In Myocardial Infarction (TIMI) flow grade 0 or 1 (21) at initial coronary angiography were considered as the study population. The diagnosis of AMI was made on the basis of chest pain of >30 min duration, ST-segment elevation of >2 mm in 2 contiguous electrocardiographic (ECG) leads and more than threefold increase in serum creatine phosphokinase activities. Patients were excluded from the study for the following reasons: cardiogenic shock or hypotension, defined as systolic blood pressure <80 mm Hg (3 patients were excluded); prior myocardial infarction (4 patients); multivessel disease (5 patients); and need for mechanical support (intra-aortic balloon pumping, mechanical ventilation, or both) (4 patients). Therefore, this report is based on the remaining 50 patients. All patients underwent percutaneous coronary intervention (PCI) and achieved successful coronary reflow (TIMI flow grade 2 or 3) within 6 hours after the symptom onset. The study was approved by the ethics review board of our institution, and informed written consent was obtained from all patients.

**Study protocol.** This is a prospective randomized study (double-blind, 1:1 ratio). After establishing a diagnosis of AMI, we randomly assigned the patients to receive either ANP (group A; n = 25) or isosorbide dinitrate (ISDN) (group B; n = 25). After the patient arrived in the CCU and hemodynamic stability was assured, ANP was continuously infused at 0.025 µg/kg/min in group A, and ISDN was continuously infused at 0.67 µg/kg/min in group B. After the start of ANP or ISDN continuous infusions, all patients underwent cardiac catheterization with the femoral approach after an injection of 100 U/kg of heparin. The infarct-related artery was visualized in five views with contrast injections, and patency was determined according to the TIMI classification. Patients who had persistent occlusion of the infarct-related vessel (TIMI flow grade 0 or 1) underwent PCI standard techniques.

Data on additional electrocardiographic ST-segment elevation and reperfusion arrhythmias were collected at the time of reperfusion. The following arrhythmias not observed before reperfusion were regarded as reperfusion arrhythmias: accelerated idioventricular or atrioventricular junctional rhythms, ventricular tachycardia (at least 3 consecutive beats), and ventricular fibrillation.

After angioplasty, ANP or ISDN was continuously infused >48 h. All patients received oral aspirin and ticlopidine. Moreover, oral angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, beta-adrenergic blocking agents, and/or diuretics were added and continued.

We performed resting $^{201}$Tl and $^{99m}$Tc-pyrophosphate (PYP) dual single-photon emission computed tomography (SPECT) imaging to evaluate the area of initial myocardial damage 3 to 5 days after primary angioplasty. Follow-up coronary angiography and left ventriculography (right anterior oblique 30°) were performed 2 weeks after angioplasty. At our institution, follow-up catheterization is routinely performed 2 weeks after angioplasty in patients with AMI. Left ventricular end-diastolic pressure (LVEDP) was determined from a transducer connected to a pig-tail catheter just before left ventriculography. The left ventricular end-diastolic volume (LVEDV) and LVEF were calculated by the area-length method. These measurements were performed by an independent observer in a blinded manner. The $^{123}$I-MIBG scintigraphy was performed 3 weeks later.

**Cardiac $^{123}$I-MIBG scintigraphy.** The method of $^{123}$I-MIBG imaging has been described previously (14–20). Briefly, the $^{123}$I-MIBG was obtained from a commercial source (Daiichi Radioisotope Laboratories, Tokyo, Japan). At 15 min and at 4 h after injection, the anterior planar and SPECT images were obtained with a single-head gamma camera (Millennium MPR, GE Medical Systems, Waukesha, Wisconsin).

The heart/mediastinum count (H/M) ratio was determined from the anterior planar delayed $^{123}$I-MIBG image. The washout rate (WR) was calculated from early and delayed planar images. Regional tracer uptake was assessed semiquantitatively using a 5-point scoring system.
(0 = normal to 4 = no uptake) in 17 segments of delayed SPECT image, as recommended by the American Heart Association (22). The total defect score (TDS) was calculated as the sum of all defect scores.

**Resting $^{201}$Tl and $^{99m}$Tc-PYP dual SPECT.** The method of $^{201}$Tl and $^{99m}$Tc-PYP dual SPECT has been described previously (23). In brief, each patient received 740 MBq of $^{99m}$Tc-PYP intravenously and then 74 MBq of $^{201}$Tl 2 h later. Fifteen minutes after the $^{201}$Tl injection, all patients underwent myocardial imaging with dual SPECT with the same system. For each patient, these images were divided into 17 segments by the same method used for $^{123}$I-MIBG imaging. We evaluated the myocardial perfusion SPECT abnormalities of $^{201}$Tl by using the TDS calculated by the same method. Furthermore, the extent score (ES) was determined from $^{99m}$Tc-PYP as the sum of the area of abnormal uptake for all 17 segments.

**Statistical analysis.** Statistical analysis was performed by using SPSS 12.0 for Windows (SPSS Inc., Chicago, Illinois). Numerical results are expressed as mean ± SD. Comparison of baseline categoric data between the 2 groups was done by the chi-square test, and differences between continuous variables were evaluated using the unpaired t test. The reperfusion phenomenon of additional electrocardiographic ST-segment elevation and reperfusion arrhythmias were expressed as percentages and compared by Fisher exact test. A value of p < 0.05 was considered to be statistically significant.

**Results**

**Clinical characteristics.** No significant differences were observed in clinical characteristics between the subjects in the 2 groups on entry into the study. Age, gender, recanalization time, and peak creatine phosphokinase levels in the acute phase were similar for both groups (Table 1). The mean duration of ANP administration was 56 ± 15 h (range 48 to 96 h) in group A, and that of ISDN administration was 59 ± 16 h (range 48 to 96 h) in group B. There were also no differences in the in-hospital medications between the 2 groups. The mean dose of enalapril was 8.2 ± 2.8 mg/day in group A versus 8.5 ± 3.0 mg/day in group B (p = NS). The mean dose of perindopril was 2.6 ± 1.2 mg/day in group A versus 2.5 ± 1.4 mg/day in group B (p = NS). The mean dose of valsartan was 104 ± 54 mg/day in group A versus 93 ± 55 mg/day in group B (p = NS). The mean dose of carvedilol was 12 ± 5 mg/day in group A versus 11 ± 4 mg/day in group B (p = NS). The mean dose of furosemide was 30 ± 12 mg/day in group A versus 31 ± 14 mg/day in group B (p = NS). Finally, the dose of spironolactone was only 25 mg/day in both groups. Other in-hospital therapies and clinical follow-up were similar in both groups.

**Comparison of reperfusion phenomenon.** The incidence of additional electrocardiographic ST-segment elevation in group A was significantly lower than in group B (20% vs. 35%; p < 0.05), and that of reperfusion arrhythmias in group A was also lower than in group B (28% vs. 48%; p < 0.05).

**Comparison of cardiac $^{201}$Tl and $^{99m}$Tc-PYP dual SPECT.** Table 1 provides a summary of the ES and TDS data for both groups as evaluated by cardiac $^{201}$Tl and $^{99m}$Tc-PYP dual SPECT. From this dual SPECT, we confirmed that all patients had first anterior AMI, and there were no patients with prior myocardial infarction. The ES evaluated from $^{99m}$Tc-PYP was similar in both groups. However, the TDS of $^{201}$Tl in group A was significantly lower than in group B (p < 0.01).

**Comparison of left ventricular parameters 2 weeks after treatment.** Table 1 presents a summary of the ES and TDS data evaluated by cardiac $^{201}$Tl and $^{99m}$Tc-PYP dual SPECT. From this dual SPECT, we confirmed that all patients had first anterior AMI, and there were no patients with prior myocardial infarction. The ES evaluated from $^{99m}$Tc-PYP was similar in both groups. However, the TDS of $^{201}$Tl in group A was significantly lower than in group B (p < 0.01). The H/M ratio, and WR are shown in Figure 1. The TDS in group A was significantly lower than in group B (p < 0.05). The H/M ratio in group A was significantly higher than in group B (p < 0.01).

**Comparison of cardiac $^{123}$I-MIBG scintigraphic findings 3 weeks after treatment.** The TDS, H/M ratio, and WR are shown in Figure 1. The TDS in group A was significantly lower than in group B (p < 0.05). The H/M ratio in group A was significantly higher than in group B (p < 0.01).

Table 1: Clinical Characteristics and LV Parameters of Patients in Both Groups

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group A (n = 25)</th>
<th>Group B (n = 25)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>61 ± 12</td>
<td>62 ± 13</td>
<td>0.78</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>20 (80.0%)</td>
<td>19 (76.0%)</td>
<td>0.73</td>
</tr>
<tr>
<td>Female</td>
<td>5 (20.0%)</td>
<td>6 (24.0%)</td>
<td>0.73</td>
</tr>
<tr>
<td>History of stroke</td>
<td>2 (8.0%)</td>
<td>1 (4.0%)</td>
<td>0.55</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>7 (28.0%)</td>
<td>6 (24.0%)</td>
<td>0.74</td>
</tr>
<tr>
<td>Hypertension</td>
<td>14 (56.0%)</td>
<td>13 (52.0%)</td>
<td>0.77</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>8 (32.0%)</td>
<td>9 (36.0%)</td>
<td>0.77</td>
</tr>
<tr>
<td>Current smoker</td>
<td>14 (56.0%)</td>
<td>15 (60.0%)</td>
<td>0.77</td>
</tr>
<tr>
<td>Recanalization time (h)</td>
<td>3.7 ± 1.5</td>
<td>3.9 ± 1.8</td>
<td>0.67</td>
</tr>
<tr>
<td>TIMI flow grade 3</td>
<td>23 (92.0%)</td>
<td>23 (92.0%)</td>
<td>1.00</td>
</tr>
<tr>
<td>TIMI flow grade 2</td>
<td>2 (8.0%)</td>
<td>2 (8.0%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Stent</td>
<td>23 (92.0%)</td>
<td>22 (88.0%)</td>
<td>0.64</td>
</tr>
<tr>
<td>Peak CPK (IU/l)</td>
<td>2,959 ± 1,648</td>
<td>3,187 ± 1,891</td>
<td>0.65</td>
</tr>
<tr>
<td>In-hospital medications</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACE inhibitor</td>
<td>23 (92.0%)</td>
<td>23 (92.0%)</td>
<td>1.00</td>
</tr>
<tr>
<td>ARB</td>
<td>5 (20.0%)</td>
<td>6 (24.0%)</td>
<td>0.73</td>
</tr>
<tr>
<td>Beta-blocker</td>
<td>21 (84.0%)</td>
<td>22 (88.0%)</td>
<td>0.68</td>
</tr>
<tr>
<td>Loop diuretics</td>
<td>5 (20.0%)</td>
<td>6 (20.0%)</td>
<td>0.73</td>
</tr>
<tr>
<td>Spironolactone</td>
<td>2 (8.0%)</td>
<td>2 (8.0%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Extent score of $^{99m}$Tc-PYP</td>
<td>9 ± 3</td>
<td>9 ± 4</td>
<td>1.00</td>
</tr>
<tr>
<td>Total defect score of T1-201</td>
<td>27 ± 7</td>
<td>32 ± 6</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>LVEDP (mm Hg)</td>
<td>11.2 ± 4.3</td>
<td>12.1 ± 6.8</td>
<td>0.58</td>
</tr>
<tr>
<td>LVEDV (ml)</td>
<td>85.5 ± 28.5</td>
<td>106.3 ± 39.4</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>47.9 ± 10.2</td>
<td>41.5 ± 11.8</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Data are presented as the mean ± SD.

ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; CPK = creatine phosphokinase; LVEDP = left ventricular end-diastolic pressure; LVEDV = left ventricular end-diastolic volume; LVEF = left ventricular ejection fraction; TIMI = Thrombolysis In Myocardial Infarction; $^{99m}$Tc-PYP = $^{99m}$Tc-pyrophosphate.
Finally, the WR in group A was significantly lower than in group B (p < 0.005). Representative 123I-MIBG images for both groups 3 weeks after reperfusion therapy are shown in Figures 2 and 3.

Discussion
Our findings demonstrate for the first time that intravenous administration of ANP could improve cardiac sympathetic nerve activity and prevent left ventricular remodeling to a larger extent compared with ISDN after reperfusion therapy in patients with first anterior AMI.

Reperfusion of the ischemic myocardium by PCI reduces the size of the infarct and improves LV function, both of which contribute to an improved clinical outcome for patients with AMI (24,25). However, in some patients who undergo reperfusion therapy, reperfusion per se adversely leads to tissue damage known as reperfusion injury (26). Intravenous administration of ANP is a promising candidate for an adjunctive therapy for AMI, because it can suppress the RAAS and endothelin-1, both of which modulate cardiac remodeling (9,27). On the other hand, ischemic preconditioning is a phenomenon in which brief periods of ischemia confer cardioprotective effects against prolonged ischemia (28). Gross and Auchampach (29) reported that ischemic preconditioning produces cardioprotection via activation of adenosine triphosphate (ATP)-sensitive potassium channels. Pharmacologic opening of the channel mimics ischemic preconditioning, whereas closing the channel blocks cardioprotection (30). Atrial natriuretic peptide is a known ATP-sensitive potassium channel activator (30); therefore, this agent may have ischemic preconditioning effect during ischemia reperfusion. Moreover, Das et al. (31) have discussed that an ATP-sensitive potassium channel activator exhibits cardioprotective effects against reperfusion injury in the myocardium. In that report, selective activation of mitochondrial ATP-sensitive potassium channels increased survival rate and decreased the incidence of arrhythmias. In the present study, the incidence of additional electrocardiographic ST-segment elevation and reperfusion arrhythmias was lower in the ANP group than in the ISDN group. Atrial natriuretic peptide may therefore have cardioprotective effects against reperfusion injury in patients with AMI.

Currently, nuclear imaging with 99mTc-PYP scintigraphy is used to measure the area of initial myocardial damage after AMI (32,33). A significant correlation has been reported between myocardial 99mTc-PYP scintigraphic uptake and the area at risk in cases of myocardial infarction (34). Because 201Tl scintigraphic uptake is known to indicate restored myocardial perfusion and cell viability, 201Tl and 99mTc-PYP dual SPECT can be useful in identifying the extent of damaged but salvaged myocardium (35). In our study, the ES evaluated by 99mTc-PYP was similar in both groups. Therefore, the initial area at risk of both groups in this study may be similar. However, defect scores from 201Tl scintigraphy were significantly lower in the ANP group than in the ISDN group. From this, we concluded that intravenous administration of ANP may increase the amount of salvaged myocardium after reperfusion therapy in patients with AMI.

123I-meta-iodobenzylguanidine, an analog of the adrenergic neuron blocking agent guanethidine, is thought to use the same mechanism of myocardial uptake and release as norepinephrine (36). An association between myocardial norepinephrine concentration and 123I-MIBG uptake in patients has been reported previously (37). Therefore, cardiac 123I-MIBG imaging may be a useful tool for detecting abnormalities of the myocardial adrenergic nervous system in patients with AMI (10). Miura et al. (38) reported that the ischemic preconditioning effect attenuates cardiac sympathetic nerve injury during myocardial isch-
Group A (ANP)

SA

VLA

HLA

Group B (ISDN)

SA

VLA

HLA

ANP = atrial natriuretic peptide; HLA = horizontal long axis; ISDN = isosorbide dinitrate; MIBG = $^{123}$I-meta-Iodobenzylguanidine; SA = short axis; VLA = vertical long axis.
emia, suggesting this effect may mediate increasing the myocardial uptake of norepinephrine. However, there are no reports on the changes in cardiac $^{123}$I-MIBG scintigraphic findings in response to ANP administration in patients with AMI. In the present study, the TDS, H/M ratio, and WR determined by cardiac $^{123}$I-MIBG scintigraphy were better in the ANP group than in the ISDN group.

Buss et al. (39) reported that aldosterone directly prevents myocardial uptake of norepinephrine in experimental animal model. Moreover, in that study, the mineralocorticoid receptor antagonist spironolactone preserved cardiac norepinephrine uptake in salt-sensitive Dahl rats (39). On the other hand, ANP has been reported to inhibit aldosterone synthase gene expression in cultured neonatal rat cardiocytes (40). Thus, ANP as well as spironolactone may improve cardiac norepinephrine uptake in the failing human heart. Therefore, the present findings demonstrate for the first time that ANP could improve cardiac norepinephrine uptake evaluated by $^{123}$I-MIBG scintigraphy in patients with AMI. In the present study, because a small number of patients were having spironolactone after AMI (2 patients in each group) and the dose of this drug was similar in both groups, it is unlikely that spironolactone influenced our results.

Hayashi et al. (9) reported that ANP treatment decreases plasma aldosterone levels and suppresses increasing plasma brain natriuretic peptide (BNP) concentrations after reperfusion therapy in patients with AMI. Plasma aldosterone and BNP levels are well known as predictors of congestive heart failure after myocardial infarction (41,42). Moreover, $^{123}$I-MIBG scintigraphic findings have useful prognostic value in the failing ischemic human heart (10). Therefore, administration of ANP may be effective for the reducing incidence of heart failure after AMI. In the future, we need to evaluate comparative effects of ANP and ISDN on mortality and morbidity in the patients with AMI of this study.

Study limitations. The small number of patients with AMI included in this study was a limitation. In addition, the present study used a fixed ANP dose. Future studies must assess the dose-response effects of ANP on $^{123}$I-MIBG scintigraphic findings and LV parameters. In the present study, we did not perform Swan-Ganz catheterization to measure hemodynamic parameters after treatment. However, LVEDP was similar in the 2 groups. We believe that hemodynamic status was similar in the 2 groups and that ANP improves cardiac sympathetic nerve activity in patients with AMI. However, further studies will be required to confirm this hypothesis.

It has been reported that intravenous administration of BNP (nesiritide) decreases regional sympathetic nerve activity in patients with coronary heart failure (43). Although nesiritide is used for patients with heart failure in other

Figure 3  Representative Anterior Planar Delayed MIBG Images 3 Weeks After Treatment for Both Groups

In these 2 examples, delayed heart/mediastinum (H/M) count ratio and washout rate were 2.01 and 36%, respectively, for a patient from group A and 1.55 and 52%, respectively, for a patient from group B. Abbreviations as in Figure 2.
countries, it is not clinically used in Japan. Moreover, cardiac $^{123}$I-MIBG scintigraphy has not yet achieved broad clinical acceptance. Therefore, it is still difficult to compare the effects of intravenous administration of ANP and those of BNP on cardiac sympathetic nerve activity in the failing human heart. We need to evaluate comparative effects of ANP and BNP on cardiac sympathetic nerve activity by cardiac $^{123}$I-MIBG scintigraphy after reperfusion therapy in AMI patients in the future.

Recent clinical studies have suggested that stem cell therapy can contribute to the regeneration of infarcted myocardium and enhance neovascularization of ischemic myocardium, resulting in sustained improvement of cardiac function (44,45). However, stem cell therapy is generally expensive for clinical use. Use of ANP is safer, more feasible, and less expensive than stem cell therapy; therefore, we believe that administration of ANP after reperfusion therapy in patients with AMI should be generally applicable.

**Conclusions.** The TDS, H/M ratio, and WR as determined by cardiac $^{123}$I-MIBG scintigraphy were better in the ANP group than in the ISDN group. The ES determined by $^{99m}$Tc-PYP was similar in the 2 groups. Two weeks after treatment, LV parameters were better in the ANP group than in the ISDN group. These findings indicate that ANP can benefit cardiac sympathetic nerve activity and LV remodeling in patients with first anterior AMI.

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