Application and evaluation of sacubitril/valsartan in patients with cardiac insufficiency during perioperative period of cardiac surgery

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Abstract. Sacubitril/valsartan is the first angiotensin II receptor blocker neprilysin inhibitor, which inhibits both angiotensin II receptor and neprilysin. In recent years, a series of clinical studies have shown that sacubitril/valsartan has a good therapeutic effect on heart failure. The present study was conducted to investigate the therapeutic effect and safety of sacubitril/valsartan in patients with cardiac insufficiency during the perioperative period of cardiac surgery. A total of 59 patients were divided into two groups: Heart failure with reduced ejection fraction (HFrEF) group and heart failure with preserved ejection fraction (HFpEF) group. The therapeutic effect on patients with sacubitril/valsartan was assessed by the values of left ventricular ejection fraction (LVEF) and left ventricular end-diastolic diameter (LVED). The renal safety of patients was assessed by serum creatinine (Cr) and blood urea nitrogen (BUN). Sacubitril/valsartan decreased LVED in HFrEF group and HFpEF group. And it showed a significant increase of LVEF in the HFrEF group. There was no significant change in Cr and BUN. Sacubitril/valsartan showed a good therapeutic effect on cardiac function for the perioperative period of cardiac surgery.

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Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; ALT, alanine aminotransferase; ARB, angiotensin receptor blocker; ARNI, angiotensin II receptor blocker neprilysin inhibitor; AST, aspartate aminotransferase; BNP, B-type natriuretic peptide; BUN, blood urea nitrogen; CI, confidence interval; Cr, serum creatinine; ESC, European Society of Cardiology; HFrEF, heart failure with reduced ejection fraction; LVED, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; PCI, percutaneous coronary intervention; UA, uric acid

Key words: sacubitril/valsartan, cardiac surgery, perioperative period, heart failure, cardiac insufficiency

Introduction

Heart failure is the serious and terminal stage of all kinds of cardiovascular diseases. There are one million cases of chronic heart failure per year, with five-year mortality rates as high as 50% (1). Delaying the progression of heart failure and improving the quality of life are the main treatment goals for patients with heart failure.

Sacubitril/valsartan is the first angiotensin II receptor blocker neprilysin inhibitor (ARNI), which inhibits both angiotensin II receptor and neprilysin (2). A series of clinical studies have shown that sacubitril/valsartan has a good therapeutic effect on cardiac function (3-5). Sacubitril/valsartan was approved by the US Food and Drug Administration in 2015 and was recommended for patients with heart failure by American College of Cardiology/American Heart Association/Heart Failure Society of America (6). The European Society of Cardiology (ESC) also recommends ARNI as an alternative to angiotensin-converting enzyme inhibitor (ACEI) for patients with persistent symptoms despite treatment with an ACEI, β-blocker and an angiotensin receptor blocker (ARB) or aldosterone receptor antagonist. It can reduce hospitalization and mortality (7,8).

There are few studies about the effect of sacubitril/valsartan on patients during the perioperative period of cardiac surgery. The present study focused on patients during the perioperative period of cardiac surgery with consideration of the comorbidities and concomitant medication of the patient. To explore the effect of sacubitril/valsartan on cardiac function for patients during cardiac perioperative period patients were divided into two groups: heart failure with reduced ejection fraction (HFrEF) group and heart failure with preserved ejection fraction (HFpEF) group. The present study was conducted to investigate the therapeutic effect of taking sacubitril/valsartan in patients with HFREF and HFPEF during cardiac perioperative period.

Materials and methods

The present study was an observational self-control study. The patients with heart failure who underwent cardiac surgery were recruited from Beijing Anzhen Hospital (Beijing, China). All patients were treated with sacubitril/valsartan during the perioperative period (within 7 days

prior to and following the surgery). The variations of left ventricular ejection fraction (LVEF) and left ventricular end-diastolic diameter (LVED) were evaluated at least 28 days after treatment. A total of 59 patients with heart failure between May 2019 and November 2020, were included in the present study (Table I). Patients who met the following inclusion criteria were eligible: i) ≥18 years old; ii) initiation of sacubitril/valsartan therapy during the cardiac perioperative period (within 7 days prior to and following the surgery); iii) LVEF <50 or LVEF ≥50 and B-type natriuretic peptide (BNP) >35 pg/ml and/or N-terminal B-type natriuretic peptide (NT-proBNP) >125 pg/ml and any of the following: Related structural heart disease and/or diastolic dysfunction; current symptomatic heart failure. The major exclusion criteria were: i) patients succumbed during hospitalization; ii) duration of sacubitril/valsartan treatment <28 days; iii) lack of echocardiography prior to and following treatment of sacubitril/valsartan. According to the value of LVEF, 31 patients with LVEF<50% were divided into HFrEF group and 28 patients with LVEF ≥50% into HFrEF group.

The medicine was sacubitril/valsartan tablets (Novartis International AG) with a range of dosage of 25-200 mg. The present study had been approved by the Medical Clinical Research Ethics Committee of Beijing Anzhen Hospital (approval no. 201808) and patient privacy was protected. All patients signed informed consent before they were recruited. The length of follow-up was 28 days or longer by phone, email, WeChat and return visit. Baseline characteristics, liver and kidney function, BNP and echocardiogram results of the study population were recorded. The therapeutic effect on patients with sacubitril/valsartan was assessed by the values of LVEF and LVED, which were the primary endpoints. The renal safety of patients was assessed by serum creatinine (Cr) and blood urea nitrogen (BUN), which were the secondary endpoints.

Statistical analysis. Statistical analysis was performed with SPSS17.0 software (SPSS, Inc.). Normal and continuous variables were expressed as mean ± standard deviation. Data were compared by using paired t-test across the groups. Non-normal variables were expressed as quartiles. Count data were expressed as percentages. In the subgroup analysis stratified by concomitant medication, the values of variations in LVEF and LVED prior to and following treatment were compared. The values were sampled 1,000 times and the results were shown as average and 95% confidence interval (CI). The differences between subgroups were compared using unpaired t-test and expressed by $P_{interaction}$. P<0.05 was considered to indicate a statistically significant difference.

Results

Baseline characteristics of the study population. According to the inclusion and exclusion criteria, a total of 59 patients were included, 31 in HFrEF group and 28 in HFpEF group. The participants were between 20 and 80 years old with a mean age of 56.3±12.8 years. A total of 44 patients (74.5%) were male and the average BMI was 24.7±3.1 kg/m^2. As shown in Table I, concomitant medication included diuretics, digoxigenin and antihypertensive drugs. 56 (94.9%) patients were given a combination of loop diuretics; 35 (59.3%) patients were given a combination of β-blocker. A total of 45 (76.3%) patients had valvular disease including valvular insufficiency, valve prolapse and valvular stenosis, 28 (47.4%) patients had hypertension; 27 (45.7%) patients had coronary heart disease. Other complications including hypertension, coronary heart disease, type 2 diabetes mellitus, hyperlipidemia, atrial fibrillation and renal dysfunction were shown in Table I.

Baseline characteristics of laboratory examination of patients were collected. Renal function of patients was evaluated by Cr, BUN and uric acid (UA); liver function was evaluated by alanine aminotransferase (ALT) and aspartate aminotransferase (AST). Cr, BUN, UA values and follow-up duration were non-normally distributed, which were expressed by median and quartile.

As shown in Table II, the types of cardiac surgery patients underwent included heart valve replacement, coronary-artery-bypass-grafting, heart valvuloplasty, Bentall and transcatheter aortic valve implantation.

As shown in Table III, in the present study, the maintenance dose of sacubitril/valsartan was 100 mg bid in 37 (62.7%) patients and 50 mg bid in 11 (18.6%) patients.

Sacubitril/valsartan and LVEF and LVED. As shown in Fig. 1, the LVEF showed an increase of 5.5% (P<0.001) in overall patients; the LVEF increased by 10.7% (P<0.001) in the HFrEF group; there was no significant difference of LVEF in HFpEF group. The results suggested that sacubitril/valsartan could increase significantly values of LVEF and improve cardiac function of patients in HFrEF group. As shown in Fig. 2, the changes in LVEF and LVED were analyzed. The LVED decreased by 10.8 mm (P=0.001) in HFrEF group; the LVED results decreased by 10.4 mm (P=0.004) in HFpEF group. The sizes of left ventricular could be significantly decreased by sacubitril/valsartan in both groups, which indicated that sacubitril/valsartan could reverse ventricular remodeling and improve cardiac function.

Sacubitril/valsartan and concomitant medication. As shown in Fig. 3A, according to the subgroup analysis stratified by the concomitant medication, the results showed that the combination of loop diuretics, digoxin and ACEI/ARB had no significant effect on the variation of LVEF. The combination of β-blocker and spironolactone could further improve LVEF of patients on the basis of sacubitril/valsartan ($P_{interaction}$=0.011 and $P_{interaction}$=0.007). In addition, whether patients were treated with loop diuretics, β-blockers, digoxin, spironolactone and ACEI/ARB or not, the LVED of patients decreased significantly. And there was no significant difference in variation of LVED with or without concomitant medication, as shown in Fig. 3B.

Sacubitril/valsartan and renal function. As shown in Fig. 4, compared with prior treatment, the changes in Cr and BUN were no statistical significance (P_{Cr}=0.95, P_{BUN}=0.55). There were no significant changes in renal function, which indicated that sacubitril/valsartan had little effect on renal function.

Table I. Baseline characteristics of the study population.

Characteristic	Total	HFrEF	HFpEF
Cases, n	59	31	28
Mean age ± SD, years	56.3±12.8	55.3±12.9	57.1±12.8
Sex, n (%)			
Male	44 (74.6)	25 (80.6)	19 (67.9)
Female	15 (25.4)	6 (19.4)	9 (32.1)
Mean body-mass index ± SD, kg/m^2	24.7±3.1	24.7±2.9	24.7±3.4
Medical history, n (%)			
Valvular disease	45 (76.3)	19 (61.3)	26 (92.9)
Hypertension	28 (47.4)	20 (64.5)	8 (28.5)
Coronary heart disease, n (%)	27 (45.7)	20 (64.5)	7 (25.0)
Hyperlipidemia	15 (25.4)	11 (35.4)	4 (14.2)
Diabetes mellitus	10 (16.9)	7 (22.5)	3 (10.7)
Atrial fibrillation	9 (15.2)	4 (12.9)	5 (17.8)
Renal dysfunction	4 (6.7)	3 (9.6)	1 (3.5)
NYHA functional class, n (%)			
II	16 (27.1)	4 (12.9)	12 (42.8)
III	34 (57.6)	21 (67.7)	13 (46.4)
IV	9 (15.2)	6 (19.3)	3 (10.7)
Smoker, n (%)	26 (44.1)	14 (45.2)	12 (42.9)
Drinker, n (%)	18 (30.6)	10 (32.3)	8 (28.6)
History of PCI, n (%)	5 (8.4)	5 (16.1)	0 (0.0)
Concomitant medication, n (%)			
Loop diuretics	56 (94.9)	29 (93.5)	27 (96.4)
β-blockers	35 (59.3)	22 (70.9)	13 (46.4)
Digoxin	21 (35.5)	11 (35.4)	10 (35.7)
Spironolactone	12 (20.3)	10 (32.2)	2 (7.1)
ARB	3 (5.0)	0 (0.0)	3 (10.7)
ACEI	1 (1.6)	0 (0.0)	1 (3.5)
Laboratory findings			
Cr, μmol/l[a]	76.8 (63.9,92.4)	77.0 (66.5,95.8)	75.1 (61.8,89.0)
BUN, mmol/l[a]	6.8 (5.3,9.0)	6.5 (5.32,11.1)	7.0 (5.4,9.0)
UA, μmol/l	172.0±97.7	161.0±105.0	184.2±88.9
BNP, pg/ml[a]	358.0 (137.8,759.5)	470.0 (152.0,782.0)	189.0 (65.0,688.0)
AST, U/l[a]	22.0 (17.0,38.0)	23.0 (17.0,33.0)	21.5 (18.0,38.8)
ALT, U/l[a]	19.0 (14.0,35.0)	20.0 (14.0,51.0)	18.5 (12.0,32.8)
Follow-up duration/day[a]	107 (90.5,157)	109.5 (90.3,158)	106 (90.3,158)

[a]Values are expressed as median (1st, 3rd quartiles). NYHA, New York Heart Association; PCI, percutaneous coronary intervention; ARB, angiotensin receptor blocker; ACEI, angiotensin-converting enzyme inhibitor; Cr, serum creatinine; BUN, blood urea nitrogen; UA, uric acid; BNP, B-type natriuretic peptide; AST, aspartate aminotransferase; ALT, alanine aminotransferase.

Discussion

The present study included patients with cardiac dysfunction during the cardiac perioperative period, including HFrEF group (31 cases) and HFpEF group (28 cases). HFrEF was generally caused by impaired ventricular contractile function, with eccentric cardiac hypertrophy and ventricle volume overload. HFpEF was generally caused by impaired ventricular diastolic function with increased ventricular stiffness, elevated left ventricular filling pressure, concentric cardiac hypertrophy and ventricular hypertrophy (9).

The primary indicators were the variations of LVEF and LVED in echocardiography following sacubitril/valsartan therapy. LVEF is the ratio of heart stroke volume (SV) to left ventricular end-diastolic volume (EDV) and reflects the systolic function of the left ventricle. LVEF is the commonest parameter to evaluate cardiac function in patients with heart failure. Patients with heart failure were divided into three groups by LVEF including heart failure with preserved

Table II. Types of cardiac surgery.

Type of cardiac surgery	Number of patients	Percentage
HVR	15	25.42
CABG	13	22.03
HVP	9	15.26
Bentall	8	13.56
HVR + CABG	4	6.78
TAVI	4	6.78
Others	4	6.78
Bentall + CABG	2	3.39
Total	59	100.00

HVR, heart valve replacement; CABG, coronary artery bypass grafting; HVP, heart valvuloplasty; TAVI, transcatheter aortic valve implantation.

Table III. Dosage of sacubitril/valsartan.

Medication dose	Total (n=59)	HFrEF (n=31)	HFpEF (n=28)
Initial dose in mg/day, n (%)			
200	9 (15.2)	4 (12.9)	5 (17.8)
100	39 (66.1)	21 (67.7)	18 (64.2)
50	10 (16.9)	5 (16.1)	5 (17.8)
25	1 (1.6)	1 (3.2)	0 (0.0)
Maintenance dose in mg/day, n (%)			
200	10 (16.9)	5 (16.1)	5 (17.8)
150	1 (1.6)	1 (3.2)	0 (0.0)
100	37 (62.7)	19 (61.2)	18 (64.2)
50	11 (18.6)	6 (19.3)	5 (17.8)

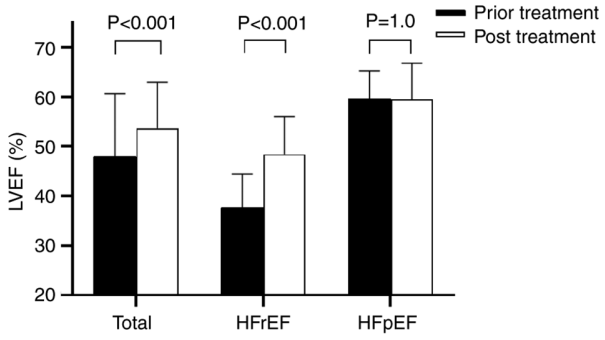

Figure 1. Effect of sacubitril/valsartan on LVEF. The variations of left ventricular ejection fraction prior to and following sacubitril/valsartan treatment in total patients, HFrEF group and HFpEF group. LVEF, left ventricular ejection fraction; HFrEF, heart failure with reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction.

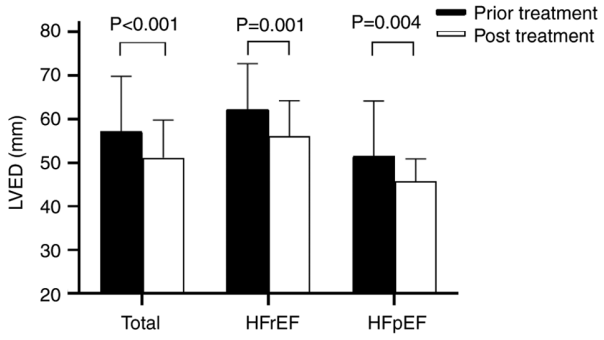

Figure 2. Effect of sacubitril/valsartan on LVED. The variations of LVED prior to and following sacubitril/valsartan treatment in total patients, HFrEF group HFpEF group. LVED, left ventricular end-diastolic diameter; HFrEF, heart failure with reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction.

ejection fraction (≥50%), heart failure with mid-range ejection fraction (40-49%) and heart failure with reduced ejection fraction (<40%). The HFrEF group in the present study included patients with heart failure mid-range ejection fraction and heart failure with reduced ejection fraction. The HFpEF group in the present study were the patients with preserved ejection fraction defined by ESC. A Meta-analysis Global Group in Chronic Heart Failure (10) collated the data from 39,372 patients data from 31 studies which showed LVEF was associated with the prognosis of heart failure and the lower the LVEF, the higher the risk of all-cause death. However, when LVEF >50%, there was no significant association between LVEF and mortality (10,11). LVED can reflect the size of the left ventricle and the degree of myocardial

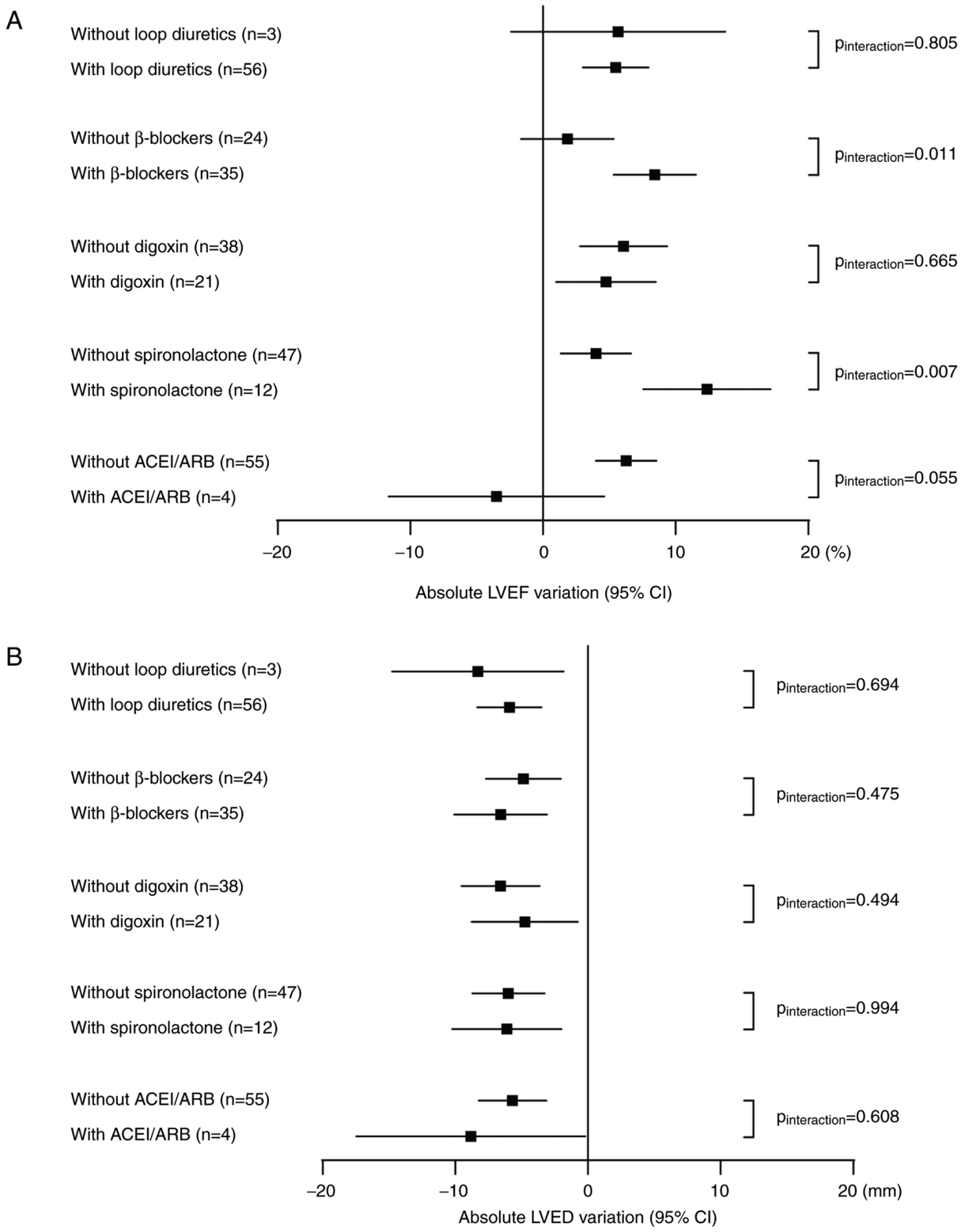

Figure 3. Effect of concomitant medication on LVEF and LVED. (A) When combined with or without other medications, the values of variations in LVEF prior to and following sacubitril/valsartan treatment were compared. (B) When combined with or without other medications, the values of variations in LVED prior to and following sacubitril/valsartan treatment were compared. LVEF, left ventricular ejection fraction; LVED, left ventricular end-diastolic diameter; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker.

remodeling. A study by Tognon *et al* (12) found that the degree of left ventricular enlargement was significantly correlated with the decline of heart function and the increase of NT-pro BNP. Therefore, in the present study, the variations of LVEF and LVED were regarded as the primary indicators for evaluating the therapeutic effect of sacubitril/valsartan on cardiac function.

The present study showed that the LVEF results of patients in HFrEF group increased significantly following sacubitril/valsartan treatment (P<0.001) and the LVED decreased

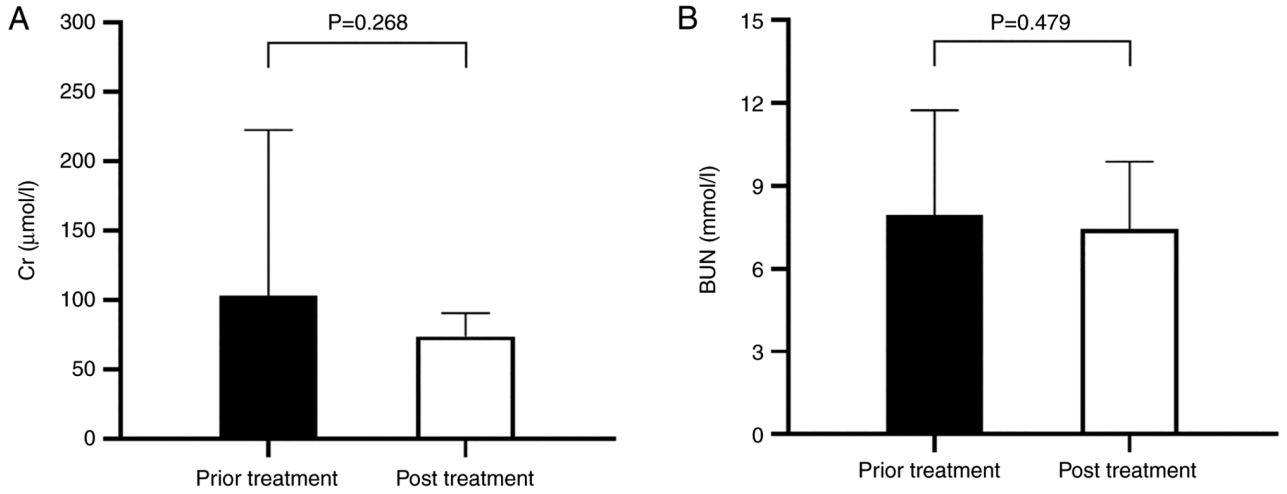

Figure 4. Effect of sacubitril/valsartan on Cr and BUN. (A) The variations of serum Cr prior to and following sacubitril/valsartan treatment in total patients. (B) The variations of BUN prior to and following sacubitril/valsartan treatment in total patients. Cr, serum creatinine; BUN, blood urea nitrogen.

significantly (P=0.001). The results suggested that sacubitril/valsartan could significantly increase the cardiac ejection function in patients with heart failure during perioperative period of cardiac surgery and reverse ventricular remodeling. Following sacubitril/valsartan treatment, there was no significant change of the LVEF value in patients of HFpEF group, but the LVED decreased significantly (P=0.001). These results suggested that sacubitril/valsartan could significantly decrease the size of the ventricle in patients with heart failure during perioperative period of cardiac surgery, reverse ventricular remodeling and improve cardiac function.

A large, randomized, double-blind, multicenter PARADIGM-HF study compared the efficacy of sacubitril/valsartan and enalapril in patients with HFrEF (13). The study included patients with New York Heart Association (NYHA) Class ~II-IV heart failure, with an LVEF ≤40% and BNP ≥150 pg/ml or NT-pro BNP ≥600 pg/ml. The primary outcome was a composite of mortality from cardiovascular causes or hospitalization for heart failure. As compared with enalapril, sacubitril/valsartan reduced the risk of hospitalization for heart failure by 21% (incidence of the composite endpoint 21.8% compared with 26.5%; hazard ratio in the sacubitril/valsartan group, 0.80; 95% CI, 0.73-0.87; P<0.001) and the results showed that sacubitril/valsartan did not increase the incidence of renal dysfunction, hyperkalemia and cough in patients, but the incidence of symptomatic hypotension increased (13-16).

There was still a high mortality rate for patients with HFpEF. However, there was a lack of effective treatments for patients with HFpEF. A randomized, double-blind, multicenter phase II clinical trial PARAGON-HF study compared the efficacy of sacubitril/valsartan and valsartan in patients with HFpEF (17). The study included patients with NYHA Class II~IV heart failure, ejection fraction of ≥45%, elevated level of natriuretic peptides and structural heart disease to receive sacubitril/valsartan or valsartan. Compared with valsartan, the difference was not statistically significant (rate ratio, 0.87; 95% CI, 0.75-1.01; P=0.06). NYHA class improved in the sacubitril/valsartan group which was higher compared with the valsartan group (15% compared with 12.6%, odds ratio, 1.45; 95% CI, 1.13-1.86) and deterioration of renal function in sacubitril/valsartan group was lower (1.4% compared with 2.7%, hazard ratio, 0.50; 95% CI, 0.33-0.77). There was no significant difference in heart failure hospitalization and cardiovascular mortality between the two groups (17,18).

The existing studies of sacubitril/valsartan were mainly on ischemic cardiomyopathy. In the sacubitril/valsartan group in PARADIGM-HF study, 59.9% of patients had ischemic cardiomyopathy and 43.4% had a history of myocardial infarction, without a history of valvular disease. In the sacubitril/valsartan group in PARAGON-HF study, 37.4% of patients had ischemic cardiomyopathy and 23.3% were hospitalized for myocardial infarction, without a history of valvular disease. In the present study, 45.7% of patients had coronary heart disease and 76.3% had a history of valvular disease. The present study mainly focused on the therapeutic effect of sacubitril/valsartan in patients with heart failure during perioperative period.

There are no reports on the treatment of sacubitril/valsartan in patients during cardiac perioperative period, to the best of the authors' knowledge. The population in the present study were patients within 7 days before and after the cardiac surgery. The results suggested that sacubitril/valsartan might serve a role in patients with cardiac insufficiency. Of 27.1% of patients with class (NYHA) II heart failure, 67.7% of patients with class (NYHA) III heart failure and 15.2% of patients with class (NYHA) IV heart failure were included in the present study. However, 71.6% of patients with class (NYHA) II heart failure in sacubitril/valsartan group, 23.1% of patients with class (NYHA) III heart failure and 0.8% of patients with class (NYHA) IV heart failure were included in PARADIGM-HF study. In total, 77.5% of patients with class (NYHA) II heart failure in sacubitril/valsartan group, 19.0% of patients with class (NYHA) III heart failure and 0.3% of patients with class (NYHA) IV heart failure were included in PARAGON-HF study. Most patients in the present study were class (NYHA) III heart failure and had the worse cardiac function. The patients usually had low blood pressure following cardiac surgery, so the initial dose of the sacubitril/valsartan was restricted. The low maintenance dose of sacubitril/valsartan might be associated with the lack of poor compliance and

regular follow-up. Therefore, was difficult to reach the target dose of sacubitril/valsartan of 200 mg bid. Only 11 (18.6%) patients finally reached the target dose in the present study. The LVEF and LVED improved significantly, even if the lower dose might not fully reflect the efficacy of sacubitril/valsartan. The lower dose of sacubitril/valsartan might have a certain therapeutic effect on heart failure.

Sacubitril/valsartan decomposes to sacubitril and valsartan in body. Valsartan is a selective AT 1 blocker that inhibits angiotensin-II-dependent aldosterone release (19). Therefore, other medications that inhibit the renin aniotension aldosterone system should avoid combining with sacubitril/valsartan, which increases the risk of angioedema without improving outcomes (20,21). There were three (5.0%) patients in the present study combined with ARB and one (1.6%) patient combined with ACEI. This combination should be avoided as much as possible to reduce the risk of angioedema in patients. No significant drug interactions were observed between sacubitril/valsartan and other commonly used medicines for heart failure and there was no induction or inhibition of Cytochrome P450 (CYP450) (22,23). In the present study, subgroup analysis was conducted considering the effect of concomitant medication on the results. Diuretics and β-blockers are first-line drugs for the treatment of heart failure (24,25). The results showed that there were only significant differences in variation of LVEF when combined with β-blocker and spironolactone, while the combination of other drugs had no significant effect on the variation of LVEF and LVED. These results did not reverse the conclusions of the whole study, which suggested that β-blocker and spironolactone could further improve LVEF of patients on the basis of sacubitril/valsartan. As for the weight of each medication for the treatment of patients with heart failure, further large sample studies are still needed.

Due to the blood pressure-lowering effect of sacubitril/valsartan, it might cause symptomatic hypotension for patients with low baseline blood pressure. In the present study, all patients started taking sacubitril/valsartan during their hospitalization and there were no drug disruptions due to cough, angioedema and hyperkalemia. On the other hand, sacubitril/valsartan had a certain effect on renal function. In the PARADIGM-HF study, 3.3% of Cr values increased by 2.5 mg/dl and 1.5% by 3.0 mg/dl in patients. There were fewer patients in the LCZ696 group compared with the enalapril group who interrupted treatment because of renal impairment (0.7% vs. 1.4%; P=0.002). Overall, there was no significant effect on Cr and BUN in the present study.

There were several limitations in the present study: i) The study was a single-center study with a small sample and lacked a randomized control group; ii) there might be confounding factors in the effect of the medicine, because the cardiac surgery itself might also affect the cardiac function of patients; iii) the bias from other concomitant medications for heart failure might affect the results of the study, thus a stratified analysis was conducted based on each combination to minimize these biases; iv) the maintenance dose of sacubitril/valsartan was low due to postoperative hypotension, poor compliance, therefore it was difficult to reach the target dose of sacubitril/valsartan of 200 mg bid and the low dose might not fully reflect the efficacy of sacubitril/valsartan; and v) due to the small sample size, the weight of each medication for the treatment of patients with heart failure and the effect of different cardiac surgeries on the results were not accessed. Therefore, large sample studies are needed in the future.

The present study explored the therapeutic effect of sacubitril/valsartan on patients with cardiac insufficiency during the perioperative period. The results showed that sacubitril/valsartan could increase the LVEF of patients with HFrEF, reduce the LVED of all patients and improve the heart function of patients. The results also indicated that there were few side effects on renal function. Furthermore, therapeutic effects were observed even with the lower dose of sacubitril/valsartan. Finally, the present study indicated that sacubitril/valsartan had a therapeutic effect on patients with cardiac insufficiency during the perioperative period, with relatively good tolerance.

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Availability of data and materials

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

Authors' contributions

WP designed the study and participated in the data analysis and manuscript writing. XL participated in analysis and interpretation of data, drafting the manuscript and manuscript writing. YL participated in writing and revising the article, and contributed to the conception of the study. WP and YL confirm the authenticity of all the raw data. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The study had been approved by the Medical Clinical Research Ethics Committee of Beijing Anzhen Hospital and patient privacy was protected (approval no. 201808). All patients provided written informed consent before they were recruited.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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