



Research Article

Perioperative Use of Sacubitril / Valsartan in Rheumatic Heart Disease Patients with Left Ventricular Dysfunction

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ABSTRACT

Background: Rheumatic heart disease (RHD) continues to be a major contributor to left ventricular dysfunction even after valvular surgery. Sacubitril/valsartan, an angiotensin receptor–neprilysin inhibitor (ARNI), is shown to be effective in heart failure management. **Objective:** To evaluate the perioperative effect of sacubitril/valsartan in improving left ventricular function in RHD patients undergoing valve surgery.

Methods: A randomized open-label study was conducted on 96 patients undergoing valve surgery. Group A (n=48) received sacubitril/valsartan perioperatively, while Group B (n=48) did not. Parameters such as LVEF, LV dimensions, NT-proBNP, and hemodynamic markers were compared. **Results:** Group A showed significant improvements in LVEF, reductions in LV dimensions and NT-proBNP levels postoperatively, compared to Group B. No significant difference in creatinine or LA size.

Conclusion: Perioperative use of sacubitril/valsartan shows potential in enhancing cardiac remodeling and function in RHD patients post valve surgery.

Keywords: Sacubitril/valsartan, Rheumatic heart disease, Left ventricular dysfunction, Valve surgery, Perioperative care.

INTRODUCTION

Heart failure (HF) is a growing global health concern, particularly among individuals with rheumatic heart disease (RHD), which remains the most common form of acquired cardiac pathology in developing countries. The hemodynamic burden from valvular lesions such as mitral and aortic regurgitation or stenosis frequently leads to left ventricular (LV) dilatation and progressive dysfunction. Despite advances in surgical interventions for valvular heart disease, a significant proportion of patients experience persistent or progressive LV dysfunction postoperatively.

Sacubitril/valsartan, an angiotensin receptor-neprilysin inhibitor (ARNI), has emerged as an effective agent in the treatment of chronic heart failure with reduced ejection fraction (HFrEF). The mechanism involves dual inhibition of neprilysin and the angiotensin receptor, promoting natriuresis, vasodilation, and ventricular remodeling. While its benefits have been established in ischemic and non-ischemic cardiomyopathy, limited evidence exists regarding its perioperative use in patients undergoing valve surgery for RHD. This study investigates the effect of perioperative administration of sacubitril/valsartan in improving cardiac remodeling and function in such patients.

AIMS AND OBJECTIVES

Aim: To evaluate the effect of perioperative sacubitril/valsartan on left ventricular function in patients with RHD undergoing valve surgery.

OBJECTIVES

1. To assess improvement in LVEF, LVEDD, and LVESD postoperatively.
2. To compare changes in NT-proBNP, blood pressure, and NYHA functional class between treatment and control groups.
3. To evaluate the safety profile of sacubitril/valsartan in the perioperative setting.

MATERIALS AND METHODS

This was a prospective, randomized, open-label study involving 96 patients undergoing cardiac valve surgery for RHD at a tertiary care center. Patients were randomized into two groups: Group A (n=48) received sacubitril/valsartan perioperatively, while Group B (n=48) did not receive the drug. Inclusion criteria was age 20–60 years and diagnosed with CHF and RHD scheduled for valve surgery and cases with ischemic heart disease or cardiogenic shock, severe arrhythmias or contraindications to sacubitril/valsartan and end-stage renal or hepatic disease were excluded from study. Preoperative, intraoperative, and postoperative parameters including HR, SBP, DBP, LVEF, LVEDD, LVESD, NT-proBNP, and NYHA grade were recorded.

Sample size calculation:

Group A : patients given treatment with sacubitril/valsartan

Group B : patients given treatment without sacubitril/valsartan

- Mean difference of the SBP in group A = $\bar{x}_1 = -13.13$
- Mean difference of the SBP in group B = $\bar{x}_2 = -1.81$
- Standard deviation of the SBP in group A = $s_1 = 23.98$
- Standard deviation of the SBP in group B = $s_2 = 10.89$
- Value of normal deviate at 95% level of confidence for two sided test = $Z_1 = 1.96$
- Value of normal deviate at 80% power of the study = $Z_2 = 0.842$
- Formula : $n = ((s_1^2 + s_2^2) * (Z_1 + Z_2)^2) / (\bar{x}_1 - \bar{x}_2)^2 = 43$ in each group
- Loss to follow up (10%) = $43 \times 10\% = 5$
- Net sample size in each group = $43 + 5 = 48$

Total sample size = 48 + 48 = 96. Hence 96 cases were included in study.

Data were analyzed using SPSS v19.0; p-values < 0.05 were considered statistically significant.

RESULTS

A total of 96 patients were included, with 48 in each group. The demographic profile (age, sex distribution) did not show any statistically significant differences between the two groups. Preoperative EF, valve pathology distribution, and surgical procedures were also similar between the groups. Notably, post-operative follow-up revealed greater improvement in Group A across several cardiac parameters:- LVEF improved more in Group A ($11.14 \pm 10.16\%$) compared to Group B ($6.65 \pm 11.18\%$) ($P < 0.05$).

- LVESD and LVEDD were reduced more significantly in Group A, although the difference in LVEDD did not reach statistical significance.
- NT-proBNP decreased significantly in Group A (-902.0 pg/ml) compared to Group B (-535.0 pg/ml) ($P < 0.05$).
- Blood pressure reduction (SBP/DBP) was more prominent in Group A ($P < 0.05$).
- NYHA functional class improvement was better in the treatment group ($P < 0.05$).

Demographic data:

No statistical significant difference between demographic data of Study group & Control group.

Table 1: Demographic data

Sociodemographic parameters	A Group (n=48)	B Group (n=48)	P value
Age (Mean $\pm$ SD)	43.20 $\pm$ 9.82	44.25 $\pm$ 11.02	Z=0.49, P > 0.05 Non Significant
Sex (M:F)	27 : 21	21 : 27	X ² = 0.006, df=1 p> 0.05 Nonsignificant

Table 2: Preoperative & Intraoperative data in the two patient groups

Parameters	A Group (n=48)	B Group (n=48)	P value
Valve Disease			
Mitral	35 (72.91%)	39 (81.25%)	$\chi^2 = 0.21$, d.f= 1, P > 0.05
Aortic	37 (77.08%)	39 (81.25%)	$\chi^2 = 0.25$, d.f= 1, P > 0.05
Tricuspid	16 (33.33%)	16 (33.33%)	$\chi^2 = 0$, d.f= 1, P > 0.05
Pre op EF (%)	60.73 $\pm$ 6.37	60.08 $\pm$ 8.25	t = 1.25, d.f= 94, P > 0.05
Surgical Procedure			

Aortic valve	11 (22.91%)	12 (25%)	$\chi^2= 0.05$, d.f= 1, P >0.05
Mitral valve	16 (33.33%)	12 (25%)	$\chi^2= 0.8$ d.f= 1, P > 0.05
Tricuspid valve	1 (2.08%)	1 (2.08%)	$\chi^2= 0.0$, d.f= 1, P >0.05
Combined Vascular Surgery	20 (41.66%)	23 (47.91%)	$\chi^2= 0.37$ d.f= 1, P > 0.05
Surgical Data			
Operative Time (min)	149 ±34.34	147.01 ±36.05	t = 1.73, d.f= 94, P > 0.05
Circulation BypassTime (min)	70.55 ±19.56	72.63 ±20.09	t = 3.17, d.f= 94, P <0.05
Aortic Clamp Time (min)	37.59 ±6.37	37.82 ±14.78	t = 0.12, d.f= 94, P > 0.05

Table 3: Prior treatment data on two groups

Paramters	A Group (n=48)	B Group (n=48)	P Value
Heart Rate (Beats/min)	83.3 ±13.9	84.4 ±17.8	t = 0.69, d.f= 94, p> 0.05
Cardiac function Grade (%)			
NYHA I	0	0	NYHA (I & II)vs NYHA (III & IV) $\chi^2= 0.38$, d.f= 1, P >0.05
NYHA II	7 (14.58%)	5 (10.41%)	
NYHA III	37 (77.08%)	38 (79.16%)	
NYHA IV	4 (8.33%)	5 (10.41%)	
SBP (mm of Hg)	127.28 ±19.75	125.11 ±15.6	t = 1.25, d.f= 94, P > 0.05
DBP (mm of Hg)	78.80 ±15.97	79.28 ±14.6	t = 0.52, d.f= 94, P <0.05
Atrial Fibrillation (%)	10 (20.83%)	6 (12.5%)	$\chi^2= 1.2$, d.f= 1, P >0.05
LVEF (%)	37.87 ±4.68	36.90 ±5.91	t = 1.92, d.f= 94, P > 0.05
LEVDD (mm)	54.13 ±6.9	54.87 ±6.2	t = 1.74, d.f= 94, P <0.05
LVESD (mm)	42.67 ±7.82	43.86 ±6.45	t = 1.88, d.f= 94, P > 0.05
LA Size (mm)	43.50 ±7.74	42.69 ±7.10	t = 1.86, d.f= 94, P > 0.05
Hb (gm/l)	122.93 ±17.25	122.84 ±14.90	t = 0.02, d.f= 94, P <0.05
Net Pro BNP (picogm/ml)	1399.0(775.0, 2814.0)	1028.0 (769.0, 2307.0)	t = 1.54, d.f= 94, P > 0.05
Se Creatinine (mg/l)	75.80 ±28.32	78.70 ±32.39	t = 0.46, d.f= 94, P > 0.05

Table 4: Follow up data in two groups

Follow up data in two groups	A Group (n=48)	B Group (n=48)	P Value
Heart Rate (Beats/min)	81.49 ±13.65	83.49 ±11.5	t = 0.77, d.f= 94, p> 0.05
Cardiac function Grade (%)			
NYHA I	13 (27.08%)	10 (20.83%)	NYHA (I & II)vs NYHA (III & IV) $\chi^2= 2.42$, d.f= 1, p< 0.05
NYHA II	24 (50%)	20 (41.66%)	
NYHA III	9 (18.75%)	14 (29.16%)	
NYHA IV	2 (4.16%)	4 (8.33%)	
SBP (mm of Hg)	114.15 ±13.01	123.31 ±12.54	t = 3.54, d.f= 94, p< 0.05

DBP (mm of Hg)	70.52 ±8.53	76.91 ±12.28	t = 2.96, d.f=94, p<0.05
LVEF (%)	49.06 ±9.96	44.05 ±9.67	t = 2.50, d.f=94, p<0.05
LEVDD (mm)	50.55 ±9.13	54.60 ±12.67	t = 1.79, d.f=94, p>0.05
LVESD (mm)	38.46 ±6.61	42.72 ±9.04	t = 2.38, d.f=94, p<0.05
LA Size (mm)	44.00 ±8.54	43.31 ±8.16	t = 0.40, d.f=94, p>0.05
Hb (gm/l)	121.08 ±16.34	119.39 ±16.13	t = 0.51, d.f=94, p>0.05
Net Pro BNP (picogm/ml)	612 (399.0, 788.0)	668.0 (435.0 , 891.5)	t = 2.54, d.f=94, p<0.05
Se Creatinine (mg/l)	75.67 ±17.14	76.23 ±17.69	t = 0.15, d.f=94, p>0.05

DISCUSSION

The findings of this study indicate that sacubitril/valsartan improves postoperative cardiac function in RHD patients undergoing valve surgery. The significant increase in LVEF, as well as reductions in NT-proBNP and ventricular dimensions, are consistent with findings from similar studies by Chang et al. (2020), who noted better recovery of LV function in non-ischemic patients treated with sacubitril/valsartan. Jian Zheng et al. (2023) similarly reported improved LVEF and LVEDD/LVESD reduction post-surgery in sacubitril/valsartan-treated patients. In our study, similar trends were observed, suggesting that perioperative ARNI therapy may have additional benefits in myocardial remodeling. Animal studies by LalidaTantisuwa et al. have also demonstrated that sacubitril/valsartan preserves mitochondrial quality and reduces myocardial fibrosis, aligning with our hypothesis of improved myocardial recovery. Our study is among the few to examine this drug in a perioperative surgical context, specifically for RHD-related HF. However, the limitations include a single-center setting and relatively short follow-up. Larger multicentric trials with long-term outcomes would help substantiate these findings.

CONCLUSION

Perioperative administration of sacubitril/valsartan significantly improves cardiac function and ventricular remodeling in patients with rheumatic heart disease undergoing valve surgery. It leads to better LVEF recovery, reduced LV dimensions, and lower NT-proBNP levels without causing significant adverse effects. Sacubitril/valsartan shows promise for broader perioperative application in non-ischemic HF.

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