Renal Replacement Therapy

CASE REPORT

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Long-term cardiac effect of sacubitril-valsartan in hemodialysis patients with a reduced ejection fraction after aortic valve replacement for aortic stenosis: a case report with literature review

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Abstract

Background Although the angiotensin receptor-neprilysin inhibitor sacubitril-valsartan has demonstrated a valuable effect on cardiac function in patients with heart failure with a reduced ejection fraction, the effect of this agent in hemodialysis patients is not well known.

Case presentation Sacubitril-valsartan was administered to two anuric hemodialysis patients, an 81-year-old woman and a 79-year-old man, after aortic valve replacement for aortic stenosis. Following sacubitril-valsartan administration, the two patients' *N*-terminal pro-brain natriuretic peptide levels decreased from 110,373 to 47,742 and 22,723 to 7692 pg/mL within one month, respectively, and were sustained within the lower levels thereafter. Although the patients' left ventricular ejection fractions were 40.0% and 28.4%, respectively, these values did not change at seven and four months after sacubitril-valsartan administration (41.0% and 30.0%, respectively) but increased gradually to 56.6% and 54.9% at 11 and 13 months, respectively, and were sustained at the same levels thereafter.

Conclusions Long-term sacubitril-valsartan administration can improve cardiac function in hemodialysis patients with a reduced ejection fraction.

Keywords Sacubitril-valsartan, Hemodialysis, Heart failure with reduced ejection fraction, *N*-terminal proBNP, Aortic stenosis, Aortic valve replacement

Background

Heart failure is associated with substantial morbidity and mortality in hemodialysis patients [1]. Recently, the angiotensin receptor-neprilysin inhibitor sacubitril-valsartan demonstrated a valuable effect in reducing the risks of hospitalizations for heart failure and death from cardiovascular causes in patients with heart failure and a reduced ejection fraction [2], which was not recognized in patients with heart failure and a preserved ejection fraction [3]. Considering that the major role of natriuretic peptides is to induce natriuresis through their action on renal hemodynamics and tubular function [4], the effectiveness of sacubitril-valsartan for improving cardiac function may not be promising in hemodialysis patients, and evidence in this population is scarce [5–10].

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We administered sacubitril-valsartan to two anuric hemodialysis patients with heart failure and a reduced ejection fraction after aortic valve replacement for aortic stenosis and considered the influences on serum natriuretic peptide levels and cardiac function of this agent in hemodialysis patients.

Case presentation

Case 1

An 81-year-old woman with IgA glomerulonephritis who had been on hemodialysis for four years and had a history of percutaneous coronary intervention, endovascular treatment of the popliteal artery and pacemaker implantation experienced syncope due to severe aortic stenosis. Aortic valve replacement (AVR) therapy was performed. Although the AVR was performed successfully, her left ventricular ejection fraction (LVEF) was 40%, and her N-terminal pro-brain natriuretic peptide (NT-proBNP) level was 110,373 pg/mL at two months after AVR. She had been administered 80 mg per day of valsartan by the time AVR was performed, and two months after AVR, 50 mg twice daily of sacubitril-valsartan was initiated and increased to 100 mg twice daily and finally to 200 mg twice daily. As shown in Fig. 1, after the administration of sacubitril-valsartan, NT-proBNP decreased from 110,373 to 47,742 pg/mL in the next month and to 18,734 pg/mL in the fourth month. The cardiothoracic ratio decreased in parallel with the decrease in NT-proBNP. Subsequently, although the NT-proBNP levels increased again, which was parallel to the increases in cardiothoracic ratio and post-hemodialysis body weight, the NT-proBNP levels were sustained at less than 40,000 pg/mL. The LVEF did not change during the half year of treatment with sacubitril-valsartan; however, it increased to 56.6% in the tenth month and was sustained at more than 50% thereafter. Hypertensive blood pressures were controlled by adjusting the dose of amlodipine, and the systolic blood pressure was controlled between 120 and 140 mmHg. Additionally, blood pressure during hemodialysis was stable. Except for the administration of valsartan, which had been initiated before AVR was performed, no cardioprotective medicines, including beta-blockers, were administered.

Case 2

A 79-year-old man with nephrosclerosis who had been on hemodialysis for seven years and had a history of percutaneous coronary intervention underwent AVR due to severe aortic stenosis. After AVR, the LVEF was consistently less than 40% and was found to be 24% 14 months later. Antihypertensive medicine, including beta-blockers, had never been administered because

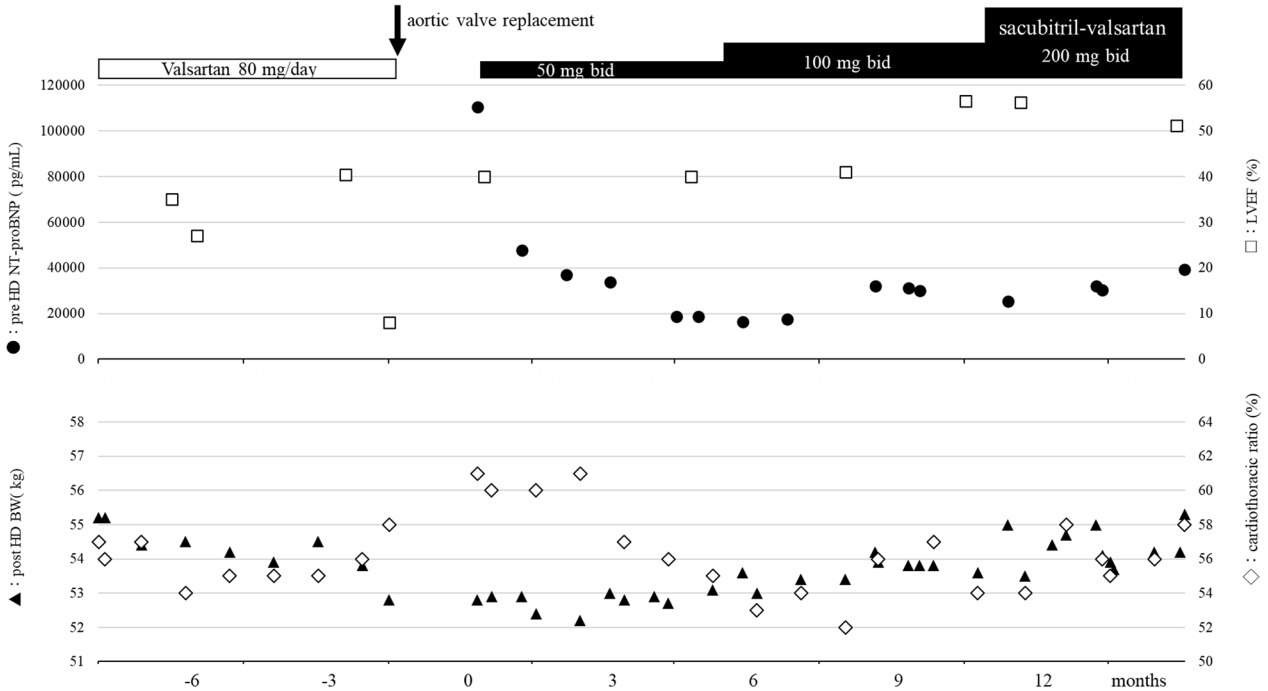

Fig. 1 Changes in the serum *N*-terminal pro-brain natriuretic peptide levels, left ventricular ejection fraction, body weight and cardiothoracic ratio before and during treatment with sacubitril-valsartan in Case 1. bid, bis in die; *HD* Hemodialysis, *NT*-Probnp, *N*-terminal pro-brain natriuretic peptide, *LVEF* Left ventricular ejection fraction, *BW* Body weight

of a risk of severe hypotension, and ivabradine had been given to control his pulse rate. After 14 months of AVR, 50 mg twice daily sacubitril-valsartan was administered. As shown in Fig. 2, after the administration of sacubitril-valsartan, NT-proBNP decreased from 22,723 to 7692 pg/mL in the next month and to 2116 pg/mL six months later. Additionally, the cardiothoracic ratio decreased in parallel with the decrease in NT-proBNP levels. After the initiation of sacubitril-valsartan, because of the temporal hypotension during the hemodialysis session, the post-hemodialysis body weight was increased, whereas the cardiothoracic ratios were between 48 and 50% and the NT-proBNP levels were between 2000 and 3000 pg/mL. Although the LVEF at the fourth month was still 30%, it increased to 47.7% at the seventh month and 54.9% at the thirteenth month and remained greater than 50% thereafter. Although the patient's blood pressures were relatively low (100–120 mmHg, systolic blood pressure), blood pressure during hemodialysis was stable and severe hypotension was not observed after the administration of sacubitril-valsartan.

We also examined the changes in NT-proBNP levels in hemodialysis patients other than the current two patients who used postoperative sacubitril-valsartan.

1. Figure 3 shows changes in the NT-proBNP levels before and after hemodialysis treatment in hemodialysis patients in our clinic.
2. Figure 4 shows changes in NT-proBNP and atrial natriuretic peptide (ANP) levels before and after arteriovenous fistula reconstruction in a 78-year-old woman on hemodialysis.
3. Figure 5 shows changes in the NT-proBNP, cardiothoracic ratio and body weight before and after the initiation of maintenance hemodialysis in a 53-year-old man with diabetic nephropathy.

Discussion

Heart failure is common in individuals with chronic kidney disease (CKD), especially in hemodialysis patients [1], and surrogate markers of cardiac stress in these populations are highly needed. Although the NT-proBNP level has been shown to predict heart failure in the general population [11], the dynamics of NT-proBNP in CKD and hemodialysis patients are different from those of the general population. Thus, for the evaluation of NT-proBNP levels in hemodialysis patients, we should pay attention to the following points.

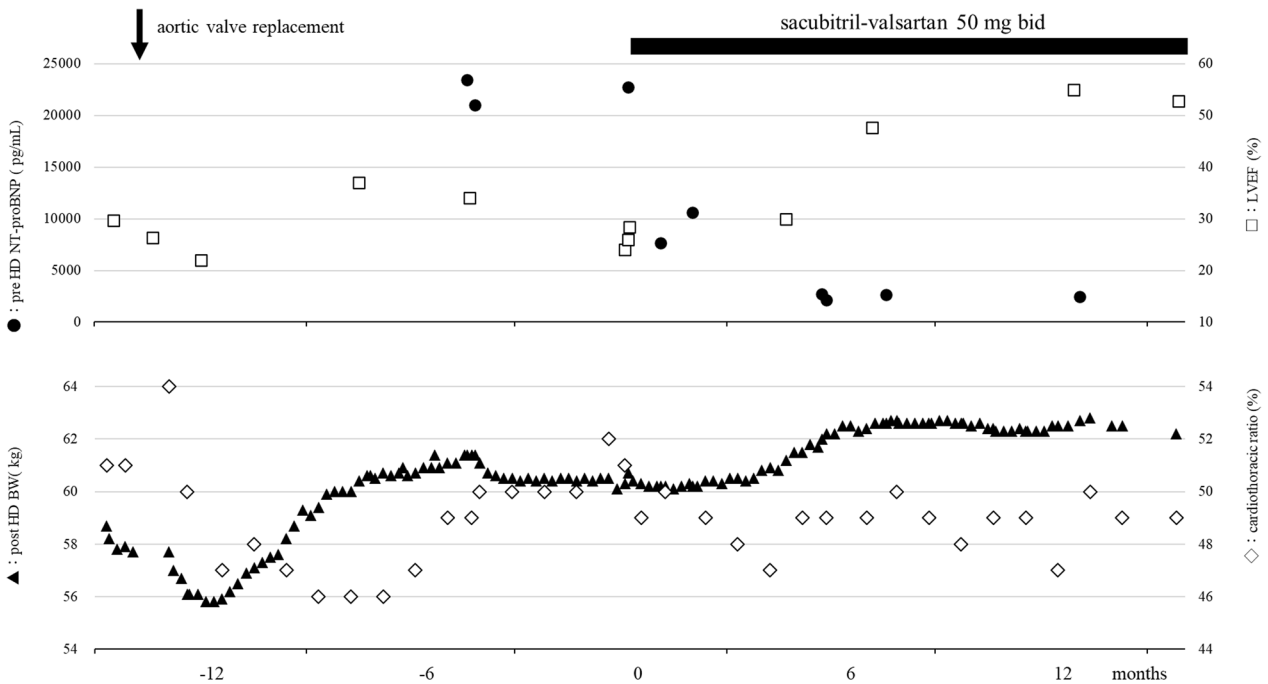

Fig. 2 Changes in the serum *N*-terminal pro-brain natriuretic peptide levels, left ventricular ejection fraction, body weight and cardiothoracic ratio before and during treatment with sacubitril-valsartan in Case 2. bid, bis in die, *HD* Hemodialysis, *NT*-proBNP, *N*-terminal pro-brain natriuretic peptide, *LVEF* Left ventricular ejection fraction; BW, body weight

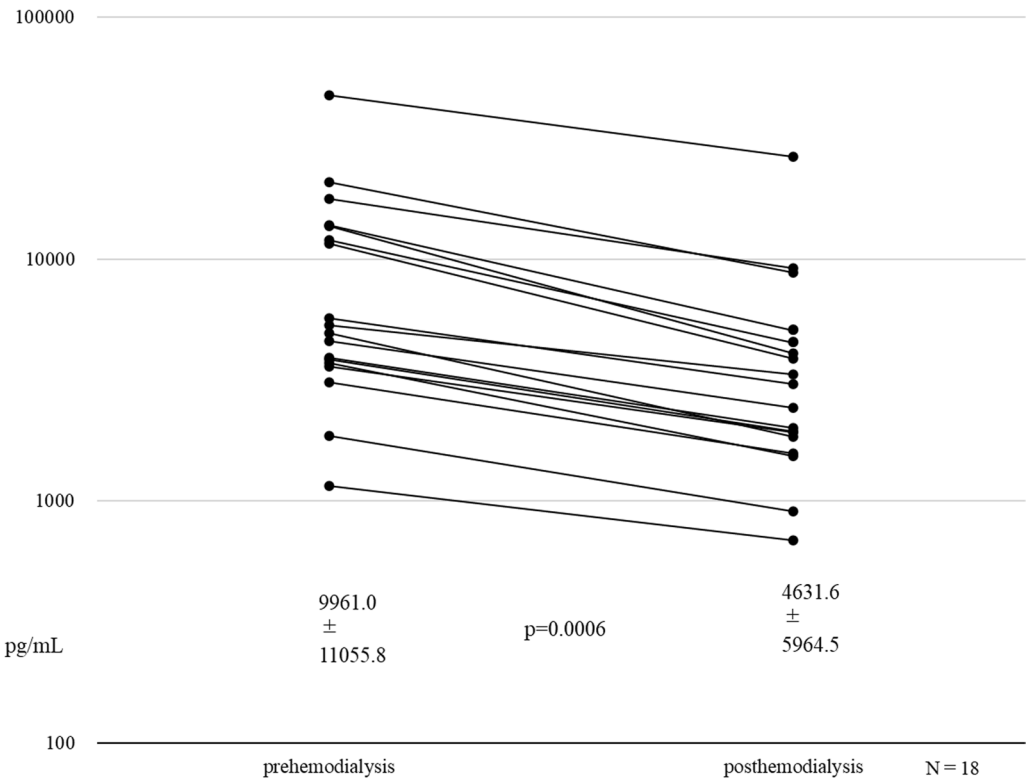

Fig. 3 Changes in the serum *N*-terminal pro-brain natriuretic peptide levels before and after hemodialysis treatment. *N* = 18

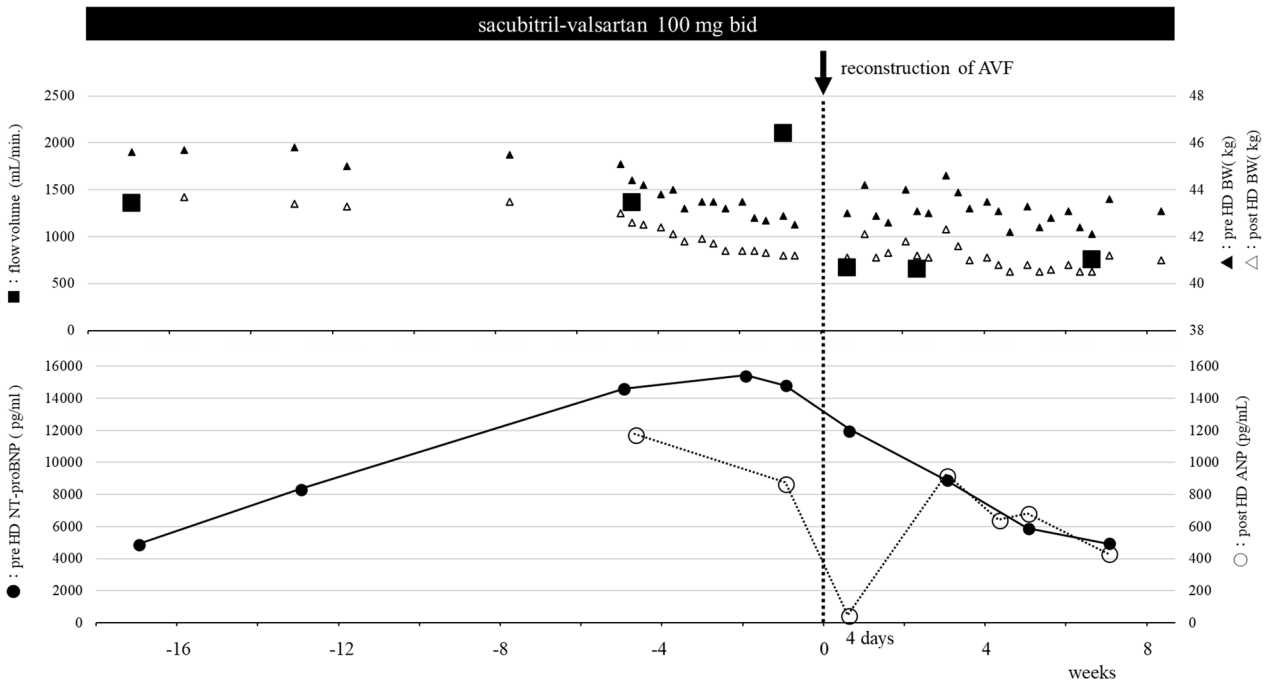

Fig. 4 Changes in serum N-terminal pro-brain natriuretic peptide levels before and after arteriovenous fistula reconstruction in a 78-year-old woman. *AVF* Arteriovenous fistula, *HD* Hemodialysis, *BW* Body weight, *NT-proBNP N*-terminal pro-brain natriuretic peptide, *ANP* Atrial natriuretic peptide

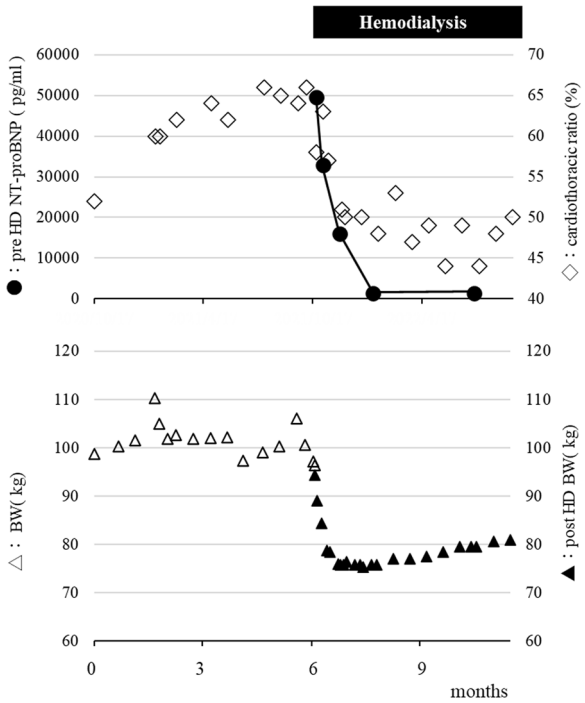

Fig. 5 Changes in the serum N-terminal pro-brain natriuretic peptide levels, cardiothoracic ratio and body weight before and after the initiation of maintenance hemodialysis in a 53-year-old man. *NT-proBNP*, *N*-terminal pro-brain natriuretic peptide, *BW* Body weight, *HD* Hemodialysis

Evaluation of natriuretic peptides levels in general population

ANP and brain natriuretic peptide (BNP) are surrogate markers of cardiac stress in normal subjects and patients with heart failure [12] and are also used to treat patients with heart failure. Although the major role of these natriuretic peptides is natriuresis [4], other roles include vasodilatation, cardiac antihypertrophic and antifibrotic effects, sympathoinhibitory effects, and aldosterone inhibition [13, 14]. Neprilysin degrades several endogenous vasoactive peptides, including angiotensin II and natriuretic peptides such as ANP and BNP. The inhibition of neprilysin increases the levels of these vasoactive peptides. By combining with valsartan, while suppressing the renin–angiotensin–aldosterone system, sacubitril-valsartan increases the natriuretic peptide levels, which then contributes to sodium and body-volume homeostasis and inhibition of cardiac maladaptive remodeling. Thus, in patients treated with sacubitril-valsartan, ANP and BNP are no longer surrogate markers of cardiac stress. The active hormone BNP and inactive fragment NT-proBNP are yielded from proBNP in a 1:1 ratio [4]. Although NT-proBNP is biologically inactive, a reduction in its serum concentration by treatment with sacubitril-valsartan in patients with reduced LVEF is significantly correlated with improvements in cardiac function [15], which indicates that the NT-proBNP concentration is a surrogate marker of cardiac stress in patients treated with sacubitril-valsartan.

Evaluation of natriuretic peptides levels in hemodialysis patients

The known mechanisms of ANP and BNP clearance from plasma include binding to the natriuretic peptide clearance receptor type-C and proteolysis by neprilysin. Renal excretion and removal of these natriuretic peptides by hemodialysis treatment have also been reported [16, 17]. Thus, for the evaluation of serum ANP and BNP levels in hemodialysis patients, the effect of reduced or absent urinary excretion and removal by hemodialysis treatment should be taken into consideration. Additionally, as mentioned above, in patients treated with sacubitril-valsartan, ANP and BNP are no longer surrogate markers of cardiac stress.

In patients with reduced kidney function, the NT-proBNP level is influenced by reduced renal excretion. In hemodialysis patients, removal by hemodialysis treatment can change the concentration of this natriuretic peptide fragment. Additionally, cardiac stress by arteriovenous fistula and volume overload due to oliguria and anuria have a substantial effect on NT-proBNP levels. Thus, for the evaluation of NT-proBNP levels in hemodialysis patients, we need a different standard compared with that in the general population.

Influences of renal function and hemodialysis treatment on serum NT-proBNP levels

As mentioned above, the known mechanisms of ANP and BNP clearance from plasma include binding to the natriuretic peptide clearance receptor type-C and proteolysis by neprilysin. On the other hand, the main mechanism of NT-proBNP clearance from plasma is renal excretion and possibly other unknown pathways [18, 19], and in patients with reduced kidney function, NT-proBNP levels are influenced by reduced renal excretion [20, 21]. Thus, when evaluating the NT-proBNP levels of hemodialysis patients, we cannot apply the reference values of the general population. Additionally, considering the molecular weight of NT-proBNP (8500), its concentration can be influenced by hemodialysis treatment. While removal by hemodialysis has been reported only to a small extent [4], Madsen et al. reported that the pre- and post-dialysis concentrations of NT-proBNP were 4079 and 2759 pg/ml, respectively (reduction ratio was 32.4%) [22]. The degree of removal may be highly influenced by the types of dialyzer membranes. Figure 3 shows changes in the NT-proBNP levels before and after hemodialysis treatment in patients in our clinic. The

reduction ratio by a single session of hemodialysis was 52.8 ± 9.4% (mean ± S.D.

Influence of cardiac stress by arteriovenous fistula on serum NT-proBNP levels in hemodialysis patients

Arteriovenous fistula is the preferred type of vascular access for maintenance hemodialysis, but it may cause some degree of cardiac stress. It has been reported that the cutoff vascular access flow value with a high predictive power for high-output cardiac failure occurrence is 2.0 L/min [23] and in the current Case 1 and 2, flow volumes of arteriovenous fistula were 382.6 and 548.6 mL/min, respectively.

However, cardiac stress induced by high flow in arteriovenous fistulas can present tremendously high NT-proBNP levels [24]. Figure 4 shows changes in NT-proBNP levels before and after arteriovenous fistula reconstruction in a 78-year-old woman who had been treated with hemodialysis for 7 years. She suffered from palpitations, shortness of breath and fatigue, and administration of sacubitril-valsartan was not effective. Her arteriovenous fistula flow volume was 2.1 L/min; after reconstruction of the fistula, the fistula flow volume decreased to 668 mL/min, and her complaints were resolved. Although ANP levels temporarily decreased drastically at 4 days after the reconstruction, they increased again by the next blood test and decreased gradually thereafter. On the other hand, NT-proBNP levels decreased consistently.

Although both ANP and BNP are natriuretic peptides produced in cardiomyocytes, there are some differences between them. Although ANP is expressed in both atrial and ventricular tissues, levels in the atria are 250–1000 times higher than those in the ventricles; thus, atria are the major source of ANP production. Under physiological conditions, although the tissue concentrations of both BNP and its mRNA are higher in the atria than in the ventricles, the total ventricular content of BNP and its mRNA correspond to ~30% and ~70% of that in the whole heart, respectively, as the ventricles are larger than the atria [25]. While plasma BNP levels are much lower than those of ANP under physiological conditions, in cases of congestive heart failure, myocardial levels of BNP mRNA and circulating levels of BNP and NT-proBNP increase against ventricular overload, which are more marked than those of ANP [18, 25]. Based on these facts, both the ANP and the NT-proBNP (but especially the NT-proBNP) levels should be influenced by the changes in cardiac stress by arteriovenous fistula flow volume. The temporal and acute decrease in ANP levels, not in NT-proBNP levels, after 4 days of fistula reconstruction may be attributed to the difference in the mechanisms of the production and secretion of these natriuretic peptides. Under cardiac stress, the production and secretion of these natriuretic peptides are stimulated, and BNP is secreted into the peripheral circulation via a constitutive pathway without storage within ventricular tissue, whereas ANP is secreted via a regulated pathway [18, 25]. Thus, ANP levels may reflect the change in cardiac stress earlier than NT-proBNP. If this is true, measuring post-dialysis ANP levels, not BNP levels, for the assessment of dry weight in hemodialysis patients [26] could be rational.

We used pre- rather than post-hemodialysis NT-proBNP for the evaluation of cardiac stress in hemodialysis patients. In a report investigating the diagnostic value of NT-proBNP for left ventricular dysfunction in patients on hemodialysis, David et al. collected blood samples during the post-hemodialysis session to correct for changes in volume status between dialysis sessions, which might affect the NT-proBNP values [27]. Although this method can minimize the influence of the changes in volume status between dialysis sessions, as mentioned above, NT-proBNP is substantially removed by hemodialysis. In the current cases, we collected pre-dialysis blood samples, which can avoid the influence of hemodialysis removal. Considering the slower changes in NT-proBNP levels than ANP levels after the fistula reconstruction mentioned above, the chance that the degree of body weight gain between hemodialysis sessions can exert a substantial influence on pre-dialysis NT-proBNP levels at the next hemodialysis session is small. Thus, we believe that except for the case using the dialyzer, which cannot remove NT-proBNP, pre- rather than post-dialysis sampling of NT-proBNP is suitable to evaluate the degree of cardiac stress in hemodialysis patients. Additionally, considering that blood work of hemodialysis patients is usually performed pre-dialysis (sometimes pre- and post-dialysis), post-dialysis sampling is not practical.

Influence of cardiac stress by volume overload on serum NT-proBNP levels in hemodialysis patients

BNP and NT-proBNP levels are influenced by volume overload [21], and the impact of volume overload on cardiac stress is extremely strong in oliguric or anuric hemodialysis patients. Figure 5 shows changes in the NT-proBNP, cardiothoracic ratio and body weight before and after the initiation of maintenance hemodialysis in a 53-year-old man with diabetic nephropathy. His urine volume was not sufficient despite diuretic administration. After the introduction of hemodialysis, his body weight and cardiothoracic ratio decreased drastically by water removal via the hemodialysis treatment. His pre-dialysis NT-proBNP level at the initiation of hemodialysis was

49,611 pg/mL, which decreased to 1411 pg/mL 96 days later.

This drastic change in NT-proBNP levels is exclusively due to the relief of cardiac stress by water removal. As shown in this case, in hemodialysis patients, the effect of volume overload on NT-proBNP levels can be augmented by the disability or inability of the urinary excretion of NT-proBNP and massive volume overload by oliguria or anuria.

Based on the above characteristics of the dynamics of NT-proBNP in hemodialysis patients, we can discuss the clinical course of Case 1 and 2, especially focused on the changes in NT-proBNP levels and LVEF before and after the administration of sacubitril-valsartan.

In non-CKD patients, prompt decreases in NT-proBNP levels after the administration of sacubitril-valsartan were reported: after four weeks in patients with heart failure and a preserved ejection fraction [28] and after two weeks in heart failure patients with a reduced ejection fraction [15]. However, it is unlikely that cardiac functional improvement occurs during such a short period, suggesting that a decrease in cardiac stress through the stimulation of diuresis and natriuresis by natriuretic peptides rather than the cardiac functional improvement might be the major mechanism of these prompt decreases in NT-proBNP levels, which cannot be expected to occur in hemodialysis patients.

In the current cases, although LVEF did not improve at least three months after the administration of sacubitril-valsartan, the NT-proBNP levels decreased rapidly within a month of administration of sacubitril-valsartan. The body weight gain between hemodialysis sessions was fairly constant in these patients (approximately 2.5 kg in case 1 and approximately 1.5 kg in case 2), and post-dialysis body weights did not change for at least three months. Thus, the acute decrease in NT-proBNP levels during the first month of sacubitril-valsartan administration may not be attributable to the relief of cardiac stress by water removal via hemodialysis. Additionally, the decrease in NT-proBNP levels by an improvement of cardiac function within a month of administration of sacubitril-valsartan is unlikely.

However, as we reported elsewhere [8] and in the current cases, a decrease in NT-proBNP levels during the first month after the administration of sacubitril-valsartan is a very common phenomenon in hemodialysis patients. Figure 6 shows changes in the serum NT-proBNP levels, hemoglobin levels, body weight, cardiothoracic ratio, and total protein and albumin levels before and after the treatment with sacubitril-valsartan in 17 hemodialysis patients. Four weeks after the administration of sacubitril-valsartan, NT-proBNP levels decreased in all the 17 patients and serum hemoglobin levels increased

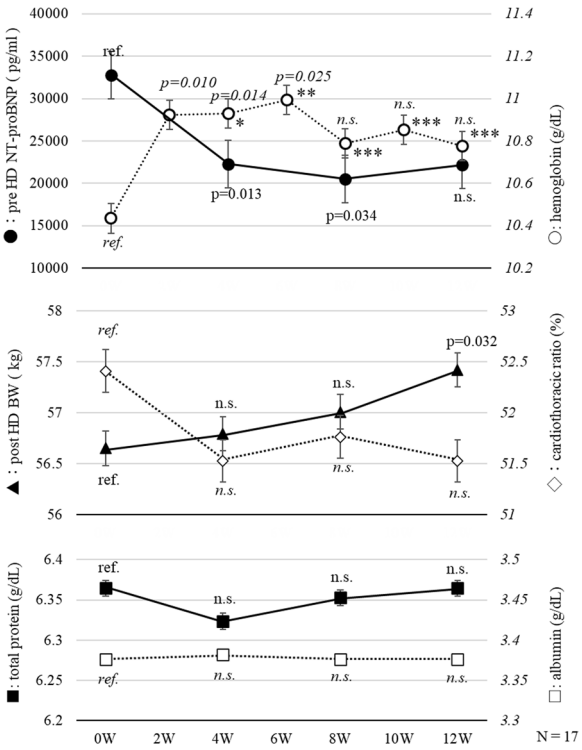

Fig. 6 Changes in the serum *N*-terminal pro-brain natriuretic peptide levels, hemoglobin, total protein, albumin,, cardiothoracic ratio, body weight and cardiothoracic ratio before and after treatment with sacubitril-valsartan. *N* = 17. *: dose of erythropoietin-stimulating agents was reduced in 2 patients. **: dose of erythropoietin-stimulating agents was reduced in 4 patients. ***: dose of erythropoietin-stimulating agents was reduced in 6 patients. *NT-proBNP*, *N*-terminal pro-brain natriuretic peptide, *HD* Hemodialysis, *BW* Body weight

significantly. Additionally, although not significant, cardiothoracic ratio tended to decrease and body weight tended to increase. These results are consistent to the hemoconcentration and resultant reduced cardiac stress. However, inconsistent with the significant increase in hemoglobin level, changes in total protein and albumin levels were insignificant. Although this is a small sample study and inconclusive, dynamics of protein, albumin and red blood cells may not be same in hemodialysis patients with sacubitril-valsartan.

ANP and BNP exert their action through stimulation of the guanylyl cyclase-A receptor. Stimulation of the guanylyl cyclase-A receptor on smooth muscle cells results in vasodilation, thereby participating in the acute regulation of blood pressure during acute hypertensive reactions under stress conditions such as hypervolemia [13]. On the other hand, stimulation of the guanylyl cyclase-A receptor on endothelial cells is critical for maintaining intravascular volume homeostasis; ANP-induced diuresis concentrates plasma proteins, and ANP facilitates

Table 1 Use of sacubitril-valsartan in hemodialysis patients: literature review

No	First author [ref. no.]	Year	No. of patients	Changes in *N*-terminal pro-brain natriuretic peptide levels		Echocardiographic findings	Ejection fraction (%)			Duration of treatment
					Duration of treatment		Pre	Post	*p*	
1	Heyse A [5]	2019	1	Decrease	3 months	Improve	N/A			
2	Lee S [6]	2020	23	N/A		Improve	29.7 ± 4.4	40.8 ± 10.4	0.002	132 days (median)
3	Lihua W [7]	2021	110	Decrease	12 months	Improve	35.1	49.8	< 0.001	12 months
4	Daimon S [8]	2022	7	Decrease	4 weeks	Improve	46.1 ± 7.9	55.9 ± 6.6	0.063	4 to 12 weeks
5	Wen Y [9]	2022	54	N/A		Improve	N/A			
6	Feng Y [10]	2022	1	N/A		Improve	18	60		3 months

microvascular albumin extravasation simultaneously [13]. This albumin extravasation may promote the shift of fluid from the intravascular space to the extravascular space and result in a decrease in intravascular volume regardless of kidney function. The prompt decrease in NT-proBNP levels concomitant with the increase in hemoglobin levels, not with total protein and albumin levels observed in Fig. 6 may indicate that a relief of cardiac stress by the shifting of the fluid from the intravascular to the extravascular space with albumin extravasation may be one of the mechanisms of the prompt decrease in NT-proBNP levels after the administration of sacubitril-valsartan. Thus, this fluid shift and also vasodilation may decrease NT-proBNP levels in hemodialysis patients receiving sacubitril-valsartan, and this does not necessarily indicate an improvement in cardiac function, particularly during the early months after the administration of sacubitril-valsartan.

Arbitrarily, the definition of left ventricular reverse remodeling was evaluated 3 to 6 months after cardiac resynchronization therapy [29], and it was reported that in non-CKD patients with heart failure and a reduced ejection fraction, the effects of sacubitril-valsartan on cardiac function were recognized after six months and were more pronounced after twelve months [15]. In the current cases, NT-proBNP levels decreased markedly within a month after the administration of sacubitril-valsartan, which may represent a relief of cardiac stress by the decrease in intravascular volume. The improvement in LVEF became apparent approximately six months after treatment with sacubitril-valsartan, suggesting that approximately six months are necessary to the time cardiac functional improvement was achieved by this agent.

Preconceptions that the increase in serum natriuretic peptide levels will not affect cardiac function in oliguric or anuric hemodialysis patients and difficulties in assessing cardiac stress by serum NT-proBNP levels in this population may make physicians reluctant to use this agent in hemodialysis patients with heart failure. Table 1 shows a list of publications on the use of sacubitril-valsartan in hemodialysis patients. In contrast to the extensive evidence that sacubitril-valsartan has a favorable cardiac effect in non-CKD patients with heart failure and a reduced ejection fraction, evidence in this population is scarce [5–10]. Lee et al. did not evaluate the changes in NT-proBNP levels because they can be largely affected by dialysis timing and duration in hemodialysis patients [6]. Additionally, as mentioned above, the NT-proBNP levels are affected by cardiac stress induced by volume status and arteriovenous fistula. Thus, NT-proBNP levels may not be an appropriate surrogate marker of cardiac function in this population. In the majority of the cases in hemodialysis patients reported to date, cardiac function was evaluated by LVEF at more than three months after the initiation of sacubitril-valsartan therapy, and improvement in cardiac function was reported [6–8, 10]. In the current case 1, sacubitril-valsartan was administered 2 months after AVR, thus it is possible that relief from cardiac stress by aortic stenosis is the cause of the increase in LVEF rather than the administration of sacubitril-valsartan. However, in case 2, sacubitril-valsartan was administered more than 1 year after AVR; which also resulted in the increase in LVEF, suggesting the possibility that this agent exerted cardiac functional improvement.

Although an antihypertensive effect of this agent in hemodialysis patients has been reported [30], the blood-lowering effect is not as strong in this population, possibly because the natriuretic effect is weak or nonexistent in hemodialysis patients; moreover, discontinuation of sacubitril-valsartan administration because of severe hypotension did not occur in hemodialysis patients in our clinic (data not shown). It seems that in the majority of cases, long-term administration of this agent to hemodialysis patients is safe.

Although the results in the current cases may not apply to general hemodialysis patients with heart failure and large-scale randomized controlled trials are needed, these findings suggest that long-term sacubitril-valsartan administration is effective for the treatment of heart failure with reduced LVEF, not only in non-CKD patients but also in oliguric or anuric hemodialysis patients.

Conclusion

Long-term sacubitril-valsartan administration has a beneficial cardiac effect in hemodialysis patients with a reduced LVEF.

Abbreviations

AVR	Aortic valve replacement
LVEF	Left ventricular ejection fraction
NT-proBNP	*N*-Terminal pro-brain natriuretic peptide
ANP	Atrial natriuretic peptide
BNP	Brain natriuretic peptide
CKD	Chronic kidney disease

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Author contributions

SD was a contributor in writing the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets generated during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee at the facility in which the studies were conducted (IRB approval number 2022 A-2) and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Consent for publication
Informed consent for publication was obtained from the individual participants included in the study.

Competing interests
The authors declare that they have no competing interests.

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