

## ORIGINAL

# The utility and limitation of inferior vena cava diameter as a dry weight marker

Eriko Shibata<sup>1</sup>, Kojiro Nagai<sup>1</sup>, Sayo Ueda<sup>1</sup>, Hiroyuki Ono<sup>1</sup>, Kenji Nishimura<sup>1</sup>, Taizo Inagaki<sup>1</sup>, Masanori Minato<sup>1</sup>, Fumi Kishi<sup>1</sup>, Masanori Tamaki<sup>1</sup>, Taichi Murakami<sup>1</sup>, Seiji Kishi<sup>1</sup>, Hideharu Abe<sup>1</sup>, Narushi Yokota<sup>2</sup>, Jun Minakuchi<sup>2</sup>, and Toshio Doi<sup>1</sup>

<sup>1</sup>Department of Nephrology, Institute of Biomedical Sciences, Tokushima University Graduate School, Japan, and <sup>2</sup>Department of Kidney Disease (Dialysis & Transplantation), Kawashima Hospital, Tokushima, Japan

**Abstract : Background :** IVC diameter on expiration (IVCdexp) is measured by echocardiography routinely. It is used to estimate volume status and designated as a definitive marker for determining dry weight (DW) in patients undergoing hemodialysis (HD). **Methods :** A cross-sectional study. Outpatients (n = 107), and inpatients (n = 35) undergoing HD were enrolled. IVCdexp was measured on non-dialysis days in outpatients and dialysis days before and after the dialysis session in inpatients. In outpatients, the relationship of IVCdexp with echocardiography findings and clinical characteristics was analyzed. IVCdexp was compared with the other DW markers as a predictive factor for intradialytic hypotension. In inpatients, IVCdexp was analyzed by dividing inpatients with or without fluid in extravascular space. **Results :** IVCdexp ranged from 5.4 to 16.9 mm in outpatients who had optimal DW. IVCdexp could reflect on volume status, but not predictive for intradialytic hypotension and not suggestive of fluid in extravascular space. **Conclusions :** IVCdexp was a rough marker to estimate volume status and only useful in suggesting apparent hypervolemia or hypovolemia. We should know that the IVCdexp value is affected by a lot of factors and not a definitive marker for estimating practical DW. *J. Med. Invest.* 66 : 172-177, February, 2019

**Keywords :** Inferior vena cava diameter, Dry weight, Hemodialysis, Intradialytic hypotension, Echocardiography

## INTRODUCTION

Dry weight (DW) is defined as the lowest tolerated postdialysis weight achieved via gradual change in postdialysis weight at which there are minimal signs or symptoms of hypovolemia or hypervolemia. The assessment of DW depends on a combination of subjective and objective measurements such as cardiothoracic ratio, intradialytic blood pressure and clinical symptoms such as dizziness and edema (1). However, DW in complicated patients such as ones after receiving invasive surgery is often difficult to determine. hANP and BNP are useful markers in patients with normal cardiac function without arrhythmia. Bioelectrical impedance analysis is also promising to estimate volume status. But the cost for these tests makes it difficult to measure them repeatedly (2). In contrast to them, inferior vena cava diameter (IVCd) is a non-invasive marker of intravascular volume status that is related to central venous pressure and circulating blood volume (3, 4). However, it is affected by right side cardiac function and tricuspid insufficiency (5, 6). Ando *et al.* proposed using the criteria of IVCd to determine DW in anuric hemodialysis (HD) patients : standard IVCd on expiration (IVCdexp) of pre- and post-HD are  $14.9 \pm 0.4$  and  $8.2 \pm 0.3$  mm, in nonoliguric HD patients : standard IVCdexp of pre- and post-HD are  $14.2 \pm 1.0$  and  $11.9 \pm 0.9$  mm (7-9). On the other hand, in the Japanese subjects who had hypertension, diabetes mellitus or dyslipidemia without obvious heart disease, IVCdexp was  $11 \pm 4$  mm, ranged from 4 to 23 mm (10). In western countries, the reference value of IVCdexp in healthy subjects was reported as around

10 to 20 mm (11, 12). However, because of the generality of IVCd measurement, inexperienced doctors sometimes believe the IVCd value definitive enough to determine DW.

Therefore, the purpose of this study is to know the utility and limitation of IVCdexp in patients undergoing HD. In outpatients undergoing HD, we measured and compared IVCdexp with other DW markers to know whether IVCdexp is useful to avoid intradialytic hypotension. In inpatients undergoing HD, we measured pre- and post-HD IVCdexp to know whether IVCdexp can be a marker for determining practical DW to reduce fluid in extravascular space.

## PATIENTS AND METHODS

### *Ethics statement*

All clinical investigations were conducted according to the principles expressed in the Declaration of Helsinki. This study was approved by the Research Ethics Committees of Tokushima University Hospital and Kawashima Hospital.

### *Study design and subjects*

This study is a cross-sectional study. One hundred and thirteen patients underwent dialysis therapy at Naruto Kawashima Clinic in September 2017. All of them were outpatients. Of these, patients (i) who had continuous arrhythmia, (ii) who had acute illness, or significant infection were initially excluded. Finally, 107 patients were included in the outpatient analysis. Fifty-five patients underwent HD and the others underwent online hemodiafiltration three times a week.

At Tokushima University Hospital, 35 inpatients who did not suffer from continuous arrhythmia were analyzed from June 2016 to June 2017. Fifteen patients were hospitalized to initiate hemodialysis (hereafter, initiation HD inpatients). The others were

Received for publication December 16, 2018 ; accepted January 22, 2019.

Address correspondence and reprint requests to Kojiro Nagai, Department of Nephrology, 3-18-15, Kuramoto-cho, Tokushima, 770-8503, Japan and Fax : +81-88-633-9245.

hospitalized because of managing acute illness and/or having an operation (hereafter, maintenance HD inpatients). Besides, 20 patients still had fluid in extravascular space such as edema and/or pleural effusion. All of them underwent HD three times a week.

In most patients, high-flux membranes with a surface area of 1.4 to 2.2 m<sup>2</sup>, were used according to clinical conditions. The ultrapure dialysate flow was fixed at 500 mL/min. The blood flow rate was between 220 and 280 mL/min and the length of each HD or HDF session was between 3.5 and 5 hours.

DW was basically assessed by intradialytic blood pressure, symptoms related to hypotension, physical examination such as edema detection and cardiothoracic ratio (CTR). Antihypertensive drugs were already reduced or removed if possible, especially in outpatients and maintenance HD inpatients.

Blood pressure was measured i) at the beginning ii) at least once an hour during the dialysis session, iii) and just after the dialysis session by oscillometric method. Intradialytic hypotension was defined as systolic blood pressure decline ≥20 mmHg or minimum systolic blood pressure ≤110 mmHg, because we had only 7 patients who had a minimum systolic blood pressure ≤100 mmHg at both dialysis sessions before and after echocardiography in outpatients (13).

Demographic and clinical characteristics were collected when IVCdexp was measured. Blood samples for biochemical data were obtained from arteriovenous shunt just before starting the first dialysis session of the week. Serum calcium concentration was adjusted for serum albumin according to the equation : corrected Ca=measured Ca+ (4.0-serum albumin in g/dL) (14).

*IVCdexp measurements by echocardiography in outpatients*

IVCdexp was measured by echocardiography on non-dialysis days in outpatients (IVCdexp of non-HD). The method was described elsewhere (15). Briefly, IVCdexp was measured in the subcostal view with the patient in the supine position at 1.0 to 2.0 cm from the junction with the right atrium, using the long-axis view. For accuracy, this measurement was made perpendicular to the IVC long axis. Intradialytic blood pressure was recorded during the dialysis sessions before and after echocardiography.

*IVCdexp measurements in inpatients*

IVCdexp was measured just before and after the dialysis session around the time of hospital discharge (IVCdexp of pre-HD and post-HD). Intradialytic blood pressure was recorded on the day IVCdexp was measured.

*Statistical analysis*

All values are expressed as mean ± SD. Statistical analysis was performed using SPSS for Windows version 13.0 (SPSS, Inc., Chicago, IL, USA). Baseline characteristics between outpatients and inpatients were compared using student's t-test or Welch's t-test, if data were normally distributed. Non-normal data were analyzed by Man-Whitney's U test. F-test was used for comparing the factors of total deviation. Prevalence data were analyzed by means of chi-square or Fisher's exact probability test. Correlation was analyzed by Pearson's correlation or Spearman's rank correlation. Significance was defined by P less than 0.05.

**RESULTS**

*Demographic and clinical characteristics*

Basic characteristics of enrolled patients were shown in Tables 1 and 2. Compared with inpatients, a higher percentage of outpatients took antihyperuricemic drugs and fewer took angiotensin II receptor blockers and warfarin. HD duration was longer in outpatients. Weight gain was larger, the levels of hemoglobin, albumin, blood

Table 1. Primary disease, comorbidity and drug profile of the patients enrolled.

	Outpatients (107)	Inpatients (35)
Primary disease	35 CGN 19 DM 12 Nephrosclerosis 8 PCK 2 Pregnancy 2 Pyelonephritis 29 Unkonwn	13 CGN 9 DM 6 Nephrosclerosis 1 PCK 1 Lupus nephritis 5 Unknown
Comorbidity		
DM (%)	38 (35.5%)	12 (34.3%)
HT (%)	55 (51.4%)	24 (68.6%)
Drug		
ARB (%)**	17 (15.9%)	12 (34.3%)
ACE-I (%)	0 (0.0%)	2 (5.7%)
Ca antagonist (%)	40 (37.4%)	17 (48.6%)
β-blocker (%)	14 (13.1%)	5 (14.3%)
α-blocker (%)	1 (0.9%)	0 (0.0%)
Vasopressor (%)	1 (0.9%)	2 (5.7%)
Anti-DM (%)	25 (23.4%)	10 (28.6%)
Statin (%)	24 (22.4%)	12 (34.3%)
Anti-UA (%)*	60 (56.1%)	4 (11.4%)
Anti-Plt (%)	57 (53.3%)	12 (34.3%)
Warfarin (%)*	4 (3.7%)	8 (22.9%)

CGN : chronic glomerulonephritis. DM : diabetes mellitus. PCK : polycystic kidney disease. HT : hypertension. ARB : angiotensin II receptor blocker.

ACE-I : angiotensin converting enzyme inhibitor. Ca antagonist : calcium antagonist. Anti-UA : antihyperuricemic drug. Anti-Plt : antiplatelet drug. \* : p <0.01. \*\* : p <0.05

urea nitrogen, creatinine, sodium, and potassium were higher and the ferritin level was lower in outpatients, suggesting outpatients had better nutritional status and less inflammation.

Among inpatients, 15 were hospitalized to initiate HD. The others usually underwent HD elsewhere and were temporally hospitalized because of receiving surgery or invasive treatment. Significantly more initiation HD inpatients showed hypertension. They had lower levels of hemoglobin, creatinine and corrected calcium and higher levels of intact PTH and IVCdexp than maintenance HD inpatients, suggesting they were still on the way to finding an optimal dialysis prescription (Table 3). Besides, 20 inpatients still had fluid in extravascular space. The inpatients with fluid were older. Weight gain was larger, albumin level was lower and ferritin level was higher, indicating they had worse nutritional and inflammatory status than those without fluid (Table 4).

*Diameter of inferior vena cava in outpatients and inpatients undergoing HD*

Figure 1 shows non-HD IVCdexp in outpatients and pre-HD IVCdexp in inpatients. The IVCdexp values were not significantly different between outpatients and inpatients (mean ± SD, 10.6 ± 2.6 mm and 11.5 ± 3.9 mm, respectively), even if around half of the inpatients still had hypertension or fluid in extravascular space and IVCdexp was measured just before starting dialysis in inpatients, while measured in non-dialysis days in outpatients. The IVCdexp values were also not different between outpatients and maintenance HD inpatients. Initiation HD inpatients had wider IVCdexp than outpatients or maintenance HD inpatients. A higher percentage of initiation HD patients manifested hypertension (Table 3), suggesting they had not reached optimal DW. Of note, not only 13.1% of outpatients, but also 28.6% of inpatients who had worse nutritional

Table 2. Demographic and clinical characteristics of the patients enrolled.

	Outpatients	Inpatients
Patients (n)	107	35
Age (years)	66.3 ± 11.1	63.6 ± 10.6
Female (%)	39 (36.4%)	16 (45.7%)
Body surface area (m <sup>2</sup> )	1.59 ± 0.18	1.54 ± 0.15
Hemodialysis duration (year)*	10.50 ± 8.16	5.31 ± 10.25
Weight gain (%DW)*	4.2 ± 1.3, 4.1 ± 1.4	3.2 ± 1.5
White blood cell (10 <sup>3</sup> /μl)	6.08 ± 1.85	6.48 ± 2.93
Hemoglobin (g/dL)*	11.1 ± 1.2	9.7 ± 1.4
Platelet (10 <sup>4</sup> /μl)**	18.1 ± 5.4	21.8 ± 10.3
AST (U/L)	15.3 ± 6.0	19.4 ± 10.4
ALT (U/L)	12.1 ± 5.4	12.9 ± 11.9
LDH (U/L)*	194 ± 44	254 ± 68
Total protein (g/dL)	6.18 ± 0.48	5.92 ± 0.74
Albumin (g/dL)*	3.45 ± 0.33	2.95 ± 0.57
Blood urea nitrogen (mg/dL)*	59.4 ± 13.8	46.5 ± 19.7
Creatinine (mg/dL)*	10.7 ± 2.7	7.0 ± 2.2
Uric acid (mg/dL)	6.17 ± 1.26	5.99 ± 1.91
Sodium (mEq/L)**	140.4 ± 2.8	139.3 ± 3.1
Potassium (mEq/L)*	4.80 ± 0.77	4.17 ± 0.63
Chloride (mEq/L)**	102.6 ± 3.7	104.1 ± 3.9
Corrected calcium (mg/dL)	9.26 ± 0.62	9.39 ± 0.82
Phosphate (mg/dL)	5.14 ± 1.04	4.82 ± 1.50
Iron (μg/dL)	60.6 ± 29.0	58.2 ± 31.3
UIBC (μg/dL)*	201.4 ± 48.7	174.9 ± 57.7
Ferritin (ng/mL)*	77.7 ± 78.7	253.6 ± 433.0
Intact PTH (pg/mL)	134.4 ± 97.0	168.8 ± 169.7

DW : dry weight. UIBC : unsaturated iron binding capacity. PTH : parathyroid hormone. \* :  $p < 0.01$ . \*\* :  $p < 0.05$ . The values of weight gain in outpatients were those at the dialysis session before and after echocardiography, respectively.

status than outpatients (Table 2) showed  $\leq 8$  mm of non-HD or pre-HD IVCdexp, which was reported as standard IVCdexp of post-HD by Ando *et al.* (7-9).

#### Relationship of DW markers with echocardiography findings, clinical characteristics and minimum systolic blood pressure in outpatients

The markers of DW such as IVCdexp, CTR (1), left ventricular end-diastolic diameter (LVDd) (16), left atrial diameter (LAD) (17) were analyzed to investigate the best marker of DW in outpatients. First, IVCdexp, LVDd and LAD were related to body surface area, so that the markers were influenced by body size. Next, IVCdexp was related to LVDd, suggesting IVCdexp measured volume status. CTR was related to not only LVDd and LAD but also IVST and PWT. Therefore, CTR reflected on both volume status and cardiac hypertrophy. LAD was also related to IVST and PWT. Considering intradialytic systolic blood pressure, LVDd had the strongest relationship with minimum blood pressure among the DW markers (Table 5).

#### The values of DW markers in outpatients with or without intradialytic hypotension

We stratified patients who experienced intradialytic hypotension during both dialysis sessions before and after echocardiography. Only LVDd was significantly different between the groups with minimum systolic blood pressure  $\leq 110$  mmHg and  $> 110$  mmHg (Table 6).

Table 3. Characteristics of inpatients undergoing the initiation of HD or maintenance HD.

	Initiation HD	Maintenance HD
Patients (n)	15	20
DM as a primary disease (%)	2 (13.3%)	7 (35.0%)
Comorbidity DM (%), HT (%)**	4 (26.7%), 13 (86.7%)	8 (40.0%), 11 (55.0%)
Age (years)	65.1 ± 8.7	62.5 ± 12.0
Female (%)	9 (60.0%)	7 (35.0%)
Body surface area (m <sup>2</sup> )	1.53 ± 0.17	1.55 ± 0.13
Hemodialysis duration (year)*	0.04 ± 0.02	9.26 ± 12.24
Weight gain (%DW)	2.7 ± 1.6	3.7 ± 1.3
SBP at the beginning (mmHg)	144.4 ± 17.7	135.2 ± 33.7
Minimum intradialytic SBP (mmHg)	121.9 ± 14.7	113.8 ± 16.2
IVCdexp. pre-*, post-HD** (mm)	13.5 ± 3.6, 11.1 ± 4.2	10.1 ± 3.4, 8.3 ± 3.5
White blood cell (10 <sup>3</sup> /μl)	6.14 ± 1.64	6.74 ± 3.63
Hemoglobin (g/dL)*	9.1 ± 1.2	10.2 ± 1.3
Platelet (10 <sup>4</sup> /μl)	19.1 ± 6.2	23.9 ± 12.3
AST (U/L)	20.5 ± 8.8	18.6 ± 11.6
ALT (U/L)	14.3 ± 8.3	11.8 ± 14.1
LDH (U/L)	273 ± 65	240 ± 68
Total protein (g/dL)	5.77 ± 0.54	6.04 ± 0.85
Albumin (g/dL)	2.95 ± 0.44	2.95 ± 0.67
Blood urea nitrogen (mg/dL)	50.5 ± 21.6	43.4 ± 18.1
Creatinine (mg/dL)**	6.1 ± 1.6	7.7 ± 2.3
Uric acid (mg/dL)	6.07 ± 1.91	5.94 ± 1.96
Sodium (mEq/L)	139.5 ± 3.0	139.1 ± 3.3
Potassium (mEq/L)	4.09 ± 0.63	4.22 ± 0.63
Chloride (mEq/L)	105.5 ± 3.8	103.1 ± 3.7
Corrected calcium (mg/dL)*	8.98 ± 0.36	9.70 ± 0.93
Phosphate (mg/dL)	4.52 ± 0.88	5.05 ± 1.84
Iron (μg/dL)	58.9 ± 22.0	57.6 ± 38.0
UIBC (μg/dL)	183.9 ± 61.0	167.5 ± 55.5
Ferritin (ng/mL)	225.4 ± 185.4	275.8 ± 561.9
Intact PTH (pg/mL)*	278.5 ± 190.3	72.0 ± 53.4

DM : diabetes mellitus. HT : hypertension. DW : dry weight. SBP : systolic blood pressure. IVCdexp : inferior vena cava diameter on expiration. HD : hemodialysis. UIBC : unsaturated iron binding capacity. PTH : parathyroid hormone.

\* :  $p < 0.01$ . \*\* :  $p < 0.05$ .

#### Diameter of inferior vena cava in inpatients undergoing HD with or without fluid in extravascular space

Inpatients were divided into those with fluid in extravascular space such as edema and/or pleural effusion and those without fluid. IVCdexp of pre-HD and post-HD in inpatients with fluid was larger than those in inpatients without fluid, but not significantly (pre-HD :  $12.3 \pm 4.1$  mm and  $10.5 \pm 3.4$  mm, respectively. post-HD :  $10.3 \pm 4.6$  mm and  $8.5 \pm 2.9$  mm, respectively.). Among inpatients with fluid, initiation HD patients had wider IVCdexp of pre-HD than maintenance HD inpatients significantly. Thirty percent of inpatients with fluid had  $\leq 8$  mm of pre-HD IVCdexp, even if we had to remove the fluid in extravascular space (Figure 2).

## DISCUSSION

In this study, we investigated the utility and limitation of IVCdexp. IVCdexp was related to volume status, but not related to intradialytic minimum blood pressure or predictive for intradialytic hypotension. IVCdexp was not significantly different between stable

Table 4. Characteristics of inpatients without or with fluid in extravascular space.

	Without fluid	With fluid
Patients (n)	15	20
DM as a primary disease (%)	4 (26.7%)	5 (25.0%)
Comorbidity DM (%), HT (%)	6 (40.0%), 11 (73.3%)	6 (30.0%), 13 (65.0%)
Age (years)*	58.6 ± 6.6	67.3 ± 11.7
Female (%)	8 (53.3%)	8 (40.0%)
Body surface area (m <sup>2</sup> )	1.56 ± 0.16	1.52 ± 0.15
Hemodialysis duration (year)	8.96 ± 14.41	2.57 ± 4.09
Weight gain (%DW)**	2.6 ± 1.5	3.7 ± 1.4
SBP at the beginning (mmHg)	144.1 ± 21.0	135.4 ± 32.3
Minimum intradialytic SBP (mmHg)	119.3 ± 13.2	115.7 ± 17.8
IVCdexp. pre-,post-HD (mm)	10.5 ± 3.4, 8.5 ± 2.9	12.3 ± 4.1, 10.3 ± 4.6
White blood cell (10 <sup>3</sup> /μl)	5.84 ± 1.64	6.96 ± 3.57
Hemoglobin (g/dL)	9.9 ± 1.3	9.7 ± 1.4
Platelet (10 <sup>4</sup> /μl)	23.4 ± 9.5	20.6 ± 10.9
GOT (U/L)	19.5 ± 12.4	19.3 ± 9.0
GPT (U/L)	13.2 ± 15.7	12.7 ± 8.5
LDH (U/L)	236 ± 42	268 ± 80
Total protein (g/dL)	6.10 ± 0.61	5.79 ± 0.81
Albumin (g/dL)*	3.29 ± 0.25	2.70 ± 0.62
Blood urea nitrogen (mg/dL)	44.3 ± 11.0	48.1 ± 24.5
Creatinine (mg/dL)	7.6 ± 2.1	6.6 ± 2.2
Uric acid (mg/dL)	5.89 ± 1.99	6.08 ± 1.89
Sodium (mEq/L)	140.1 ± 2.3	138.7 ± 3.5
Potassium (mEq/L)	4.27 ± 0.54	4.09 ± 0.69
Chloride (mEq/L)	103.9 ± 3.9	104.2 ± 4.1
Corrected calcium (mg/dL)	9.48 ± 0.84	9.33 ± 0.82
Phosphate (mg/dL)	5.19 ± 1.75	4.53 ± 1.24
Iron (μg/dL)	61.1 ± 27.0	55.9 ± 34.7
UIBC (μg/dL)*	208.2 ± 56.0	150.4 ± 46.5
Ferritin (ng/mL)**	116.5 ± 93.8	349.6 ± 544.1
Intact PTH (pg/mL)	209.1 ± 220.9	137.5 ± 113.1

DM : diabetes mellitus. HT : hypertension. DW : dry weight. SBP : systolic blood pressure. IVCdexp : inferior vena cava diameter on expiration. HD : hemodialysis. UIBC : unsaturated iron binding capacity. PTH : parathyroid hormone.

\* : *p* <0.01. \*\* : *p* <0.05.

outpatients and relatively unstable inpatients, suggesting IVCdexp was not a definitive volume status marker. IVCdexp was not significantly different between inpatients without fluid in extravascular space and those with fluid, indicating IVCdexp was not a practical DW marker.

IVCdexp was reported as an easily measurable DW marker (2). The IVCdexp value itself can be believed as a definitive marker to avoid intradialytic hypotension or symptoms of hypovolemia. In our study, IVCdexp was larger in initiation HD inpatients who did not reach optimal DW than that in maintenance HD patients (Figure 1). IVCdexp decreased after HD treatment (Figure 2). IVCdexp was related to LVDd in outpatients (Table 5). Therefore, IVCdexp could reflect on volume status. However, IVCdexp had a poor relationship with minimum intradialytic blood pressure or intradialytic hypotension (Table 6). IVCdexp did not have a correlation with interdialytic weight gain as a percentage of estimated dry weight in our outpatients (data not shown). Non-HD IVCdexp in outpatients ranged from 5.4 to 16.9 mm, and pre-HD IVCdexp in inpatients ranged from 6 to 21 mm. There is a large overlap among outpatients with optimal DW and inpatients including > 50% patients without practical DW (Figure 1, Table 3, 4). In addition, basically, inpatients have different nutritional status and hemodynamics with low serum albumin and hemoglobin concentration because of the change of diet and activity compared with outpatients (17). In this study, inpatients had lower serum albumin and hemoglobin concentration than outpatients (Table 2). It is likely that IVCdexp value itself could not be a definitive DW marker and only showed excessive hypovolemia or hypervolemia (18).

IVCdexp was body size dependent (Table 5). It is compatible with the previous report which showed a strong correlation of IVCdexp with height and weight in the normal Indian population (19). In edematous patients, IVCdexp was not significantly related to edema severity (Figure 2) (20). Therefore, we have to recognize the reference value of IVCdexp was dependent on clinical characteristics such as age, body size and comorbidities (10).

LVDd can be a better marker for assessing DW than IVCdexp. LVDd was related to minimum intradialytic blood pressure (Table 5). LVDd was significantly larger in outpatients without intradialytic hypotension than LVDd in those with intradialytic hypotension (Table 6). We guess that the LVDd values are affected by fewer factors including volume status than the IVCdexp values. Therefore, in order to avoid intradialytic hypotension, it might be better to measure LVDd than IVCdexp.

We do not deny the utility of IVCd, because we did not measure

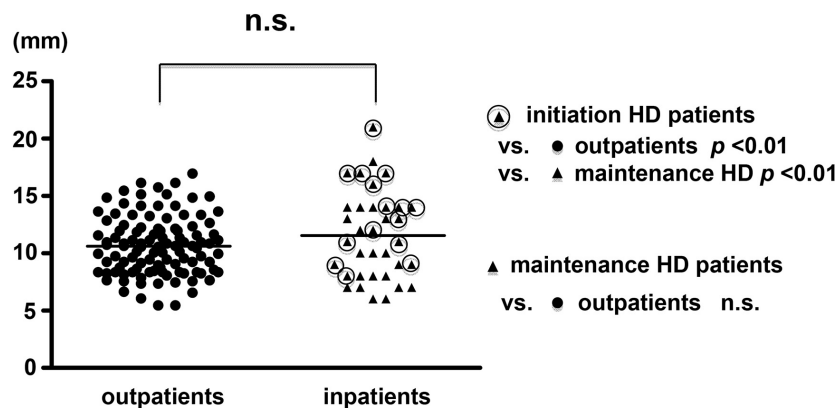


Figure 1. Inferior vena cava on expiration in outpatients and inpatients.

The inferior vena cava diameter on expiration (IVCdexp) values were not significantly different between outpatients on non-dialysis days and inpatients before starting dialysis session. The IVCdexp values were not also different between outpatients and maintenance hemodialysis (HD) inpatients. Initiation HD inpatients had wider IVCdexp than outpatients or maintenance HD inpatients significantly. Circle : outpatients. Triangle with circle : initiation HD patients. Triangle : maintenance HD patients.

Table 5. Relationship of dry weight markers with echocardiography findings, clinical characteristics and minimum systolic blood pressure in outpatients.

	IVCde	CTR	LVDd	LAD	IVST	PWT	BSA	minipr	minipost
IVCde		-0.092	0.254	0.184	-0.160	-0.169	0.256	0.203	0.121
CTR	-0.092		0.230	0.202	0.205	0.245	-0.067	-0.023	0.047
LVDd	0.254	0.230		0.355	0.130	0.187	0.427	0.345	0.228
LAD	0.184	0.202	0.355		0.308	0.353	0.329	0.277	0.179

IVCde : inferior vena cava diameter on expiration. CTR : cardiothoracic ratio. LVDd : left ventricular end-diastolic diameter. LAD : left atrial diameter. IVST : interventricular septum thickness. PWT : left ventricular posterior wall thickness. BSA : body surface area. minipr : minimum intradialytic systolic blood pressure during the dialysis session before echocardiography. minipost : minimum intradialytic systolic blood pressure during the dialysis session after echocardiography.

upright : Pearson's correlation coefficient.

oblique : Spearman's rank correlation coefficient.

hatching : correlation coefficient >0.2.

Table 6. The values of dry weight markers in outpatients with or without intradialytic hypotension.

	mSBP ≤ 110 (29)	mSBP > 110 (78)	IDH < 20 (55)	IDH ≥ 20 (52)	IDH < 30 (80)	IDH ≥ 30 (27)
IVCdex	1.01 ± 0.20	1.08 ± 0.27	1.09 ± 0.24	1.03 ± 0.27	1.08 ± 0.24	1.01 ± 0.28
CTR	49.4 ± 5.0	50.1 ± 5.4	49.8 ± 6.0	50.0 ± 4.4	49.7 ± 5.5	50.3 ± 4.7
LVDd	4.56 ± 0.45	4.76 ± 0.44**	4.73 ± 0.43	4.68 ± 0.47	4.72 ± 0.44	4.65 ± 0.47
LAD	3.79 ± 0.57	3.90 ± 0.50	3.84 ± 0.54	3.90 ± 0.50	3.85 ± 0.54	3.93 ± 0.47

mSBP : minimum intradialytic systolic blood pressure.

IDH < 20 : intradialytic hypotension less than 20 mmHg.

IVCdex : inferior vena cava diameter on expiration. CTR : cardiothoracic ratio. LVDd : left ventricular end-diastolic diameter. LAD : left atrial diameter. \*\*:  $p < 0.05$ .

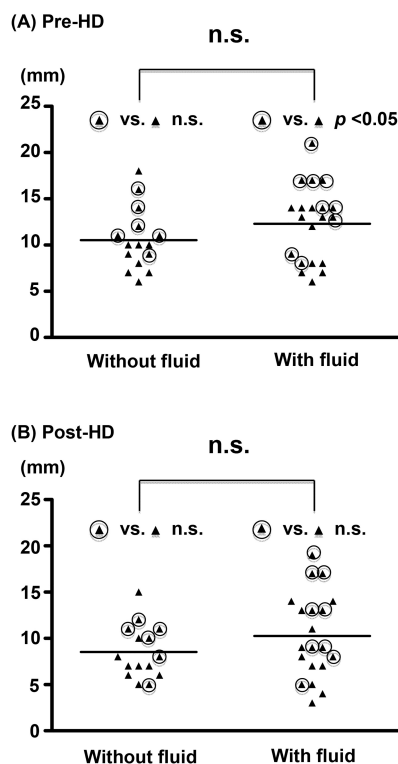


Figure 2. Inferior vena cava on expiration of pre-HD and post-HD in inpatients with or without fluid in extravascular space.

(A,B) Inferior vena cava on expiration (IVCdex) of pre-hemodialysis (HD) (A) and post-HD (B) in inpatients. IVCdex of pre-HD and post-HD in inpatients with fluid was larger than those in inpatients without fluid, but not significantly. (A) Among inpatients with fluid, initiation HD patients had wider IVCdex of pre-HD than maintenance HD inpatients significantly. Six among twenty inpatients with fluid had  $\leq 8$  mm of pre-HD IVCdex, even if we had to remove the fluid in extravascular space. Triangle with circle : initiation HD patients. Triangle : maintenance HD patients.

inspiratory collapse of IVCd. Collapsing index which is calculated by the formula :  $(\text{IVCd on expiration} - \text{IVCd on inspiration}) / \text{IVCd on expiration} * 100$ , was reported as a useful DW maker than IVCd on expiration only (21). ASE recommendation from the American Society of Echocardiography and the European Association of Cardiovascular Imaging for IVCdex and collapsing index to estimate right atrial pressure was shown previously (15). IVCdex < 21 mm that collapses > 50% with a sniff suggests normal right atrial pressure of 3 mmHg (range, 0 to 5 mmHg), whereas IVCdex > 21 mm that collapses < 50% with a sniff suggests high right atrial pressure of 15 mmHg (range, 10 to 20 mmHg) (22). The measurement of three-dimensional areas measured from cross-sectional images of the IVC may also be promising to monitor volume status (23, 24). However, collapsing index depends on the patient's effort and the variation of ultrasound results can happen among different operators (25-29). Therefore, IVCd is a rough method to estimate volume status and we should not rely on a single method to determine DW in patients undergoing HD (30).

A weakness of this study is its relatively small sample size, especially in inpatients. In addition, the timing of IVCd measurement was different between outpatients and inpatients.

In summary, in this study, we demonstrated that IVCdex could reflect on volume status, but was not a definitive marker for determining DW. The IVCd values can be suggestive to avoid apparent hypovolemia/hypovolemia, but we have to consider the patient's condition to interpret the IVCd results.

## CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

## ACKNOWLEDGEMENTS

We thank Susumu Nishio (Tokushima University Hospital) for technical advice.

## REFERENCES

- Agarwal R, Weir MR : Dry-weight : a concept revisited in an effort to avoid medication-directed approaches for blood pressure control in hemodialysis patients. *Clin J Am Soc Nephrol* 5 : 1255-1260, 2010
- Jaeger JQ, Mehta RL : Assessment of dry weight in hemodialysis : an overview. *J Am Soc Nephrol* 10 : 392-403, 1999
- Chardoli M, Ahmadi M, Shafe O, Bakhshandeh H : Inferior vena cava diameter as a guide in hypotensive patients for appropriate saline therapy : An observational study. *Int J Crit Illn Inj Sci* 8 : 160-164, 2018
- Morishita Y, Ando Y, Ishii E, Arisaka M, Kusano E : Comparison of markers of circulating blood volume in hemodialysis patients. *Clin Exp Nephrol* 9 : 233-237, 2005
- Patil S, Jadhav S, Shetty N, Kharge J, Puttegowda B, Ramalingam R, Cholenahally MN : Assessment of inferior vena cava diameter by echocardiography in normal Indian population : A prospective observational study. *Indian Heart J* 68 Suppl 3 : S26-S30, 2016
- Mandelbaum A, Ritz E : Vena cava diameter measurement for estimation of dry weight in haemodialysis patients. *Nephrol Dial Transplant* 11 Suppl 2 : 24-27, 1996
- Ando Y, Yanagiba S, Asano Y : The inferior vena cava diameter as a marker of dry weight in chronic hemodialyzed patients. *Artif Organs* 19 : 1237-1242, 1995
- Tetsuka T, Ando Y, Ono S, Asano Y : Change in inferior vena caval diameter detected by ultrasonography during and after hemodialysis. *ASAIO J* 41 : 105-110, 1995
- Yanagiba S, Ando Y, Kusano E, Asano Y : Utility of the inferior vena cava diameter as a marker of dry weight in nonoliguric hemodialyzed patients. *ASAIO J* 47 : 528-32, 2001
- Masugata H, Senda S, Okuyama H, Murao K, Inukai M, Hosomi N, Iwado Y, Noma T, Kohno M, Himoto T, Goda F : Age-related decrease in inferior vena cava diameter measured with echocardiography. *Tohoku J Exp Med* 222 : 141-147, 2010
- Rein AJ, Lewis N, Forst L, Gotsman MS, Lewis BS : Echocardiography of the inferior vena cava in healthy subjects and in patients with cardiac disease. *Isr J Med Sci* 18 : 581-585, 1982
- Nakao S, Come PC, McKay RG, Ransil BJ : Effects of positional changes on inferior vena caval size and dynamics and correlations with right-sided cardiac pressure. *Am J Cardiol* 59 : 125-132, 1987
- Assimon MM, Flythe JE : Definitions of intradialytic hypotension. *Semin Dial* 30 : 464-472, 2017
- Shigematsu T, Akizawa T, Uchida E, Tsukamoto Y, Iwasaki M, Koshikawa S : KRN1493 Study Group : Long-term cinacalcet HCl treatment improved bone metabolism in Japanese hemodialysis patients with secondary hyperparathyroidism. *Am J Nephrol* 29 : 230-236, 2009
- Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, Flachskampf FA, Foster E, Goldstein SA, Kuznetsova T, Lancellotti P, Muraru D, Picard MH, Rietzschel ER, Rudski L, Spencer KT, Tsang W, Voigt JU : Recommendations for cardiac chamber quantification by echocardiography in adults : an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *J Am Soc Echocardiogr* 28 : 1-39.e14, 2015
- Yoshimura R, Goto T, Tsuchida K, Takemoto Y, Wada S, Sano H, Kishimoto T, Yamamoto K, Nakatani T : Echography of left ventricular end-diastolic diameter as a reliable tool for estimating "dry weight" in hemodialysis patients. *Ren Fail* 25 : 31-41, 2003
- Yoshimoto S, Nagai K, Shibata E, Ueda S, Ono H, Tamaki M, Nishimura K, Obata F, Inagaki T, Minato M, Kishi F, Matsuura M, Matsui N, Endo I, Hann M, Kishi S, Murakami T, Abe H, Doi T : Influential factors on serum albumin concentration in hospitalized chronic kidney disease patients. *J Med Invest* 64 : 146-152, 2017
- Agarwal R, Bouldin JM, Light RP, Garg A : Inferior vena cava diameter and left atrial diameter measure volume but not dry weight. *Clin J Am Soc Nephrol* 6 : 1066-1072, 2011
- Patil S, Jadhav S, Shetty N, Kharge J, Puttegowda B, Ramalingam R, Cholenahally MN : Assessment of inferior vena cava diameter by echocardiography in normal Indian population : A prospective observational study. *Indian Heart J* 68 Suppl 3 : S26-S30, 2016
- Ghaffari S, Malaki M, Ghaffari MR, Asiaie K : Inferior vena cava index in edematous patients. *J Cardiovasc Thorac Res* 4 : 69-71, 2012
- Cherix EC, Leunissen KM, Janssen JH, Mooy JM, van Hooff JP : Echography of the inferior vena cava is a simple and reliable tool for estimation of 'dry weight' in haemodialysis patients. *Nephrol Dial Transplant* 4 : 563-568, 1989
- Brennan JM, Blair JE, Goonewardena S, Ronan A, Shah D, Vasaiwala S, Kirkpatrick JN, Spencer KT : Reappraisal of the use of inferior vena cava for estimating right atrial pressure. *J Am Soc Echocardiogr* 20 : 857-861, 2007
- Huguet R, Fard D, d'Humieres T, Brault-Meslin O, Faivre L, Nahory L, Dubois-Randé JL, Ternacle J, Oliver L, Lim P : Three-dimensional inferior vena cava for assessing central venous pressure in patients with cardiogenic shock. *J Am Soc Echocardiogr* 31 : 1034-1043, 2018
- Naruse M, Sakaguchi S, Nakayama Y, Nonoguchi H, Tomita K : A novel method for dry weight assessment in hemodialysis patients : Utilization of inferior vena cava flat ratio to correct for individual variations in vessel diameter. *Ther Apher Dial* 11 : 42-48, 2007
- Ng Kam Chuen MJ, Lip GY, Macfadyen RJ : Performing repeated noninvasive bedside measures of volume response to intravenous furosemide in acute pulmonary edema : a feasibility assessment. *Cardiovasc Ther* 27 : 89-95, 2009
- Goonewardena SN, Gemignani A, Ronan A, Vasaiwala S, Blair J, Brennan JM, Shah DP, Spencer KT : Comparison of hand-carried ultrasound assessment of the inferior vena cava and N-terminal pro-brain natriuretic peptide for predicting readmission after hospitalization for acute decompensated heart failure. *JACC Cardio vasc Imaging* 1 : 595-601, 2008
- Kircher BJ, Himelman RB, Schiller NB : Noninvasive estimation of right atrial pressure from the inspiratory collapse of the inferior vena cava. *Am J Cardiol* 66 : 493-496, 1990
- Schefold JC, Storm C, Bercker S, Pschowski R, Oppert M, Krüger A, Hasper D : Inferior vena cava diameter correlates with invasive hemodynamic measures in mechanically ventilated intensive care unit patients with sepsis. *J Emerg Med* 38 : 632-637, 2010
- Muniz Pazeli J, Fagundes Vidigal D, Cestari Grossi T, Silva Fernandes NM, Colugnati F, Baumgratz de Paula R, Sanders-Pinheiro H : Can nephrologists use ultrasound to evaluate the inferior vena cava? A cross-sectional study of the agreement between a nephrologist and a cardiologist. *Nephron Extra* 4 : 82-88, 2014
- Brennan JM, Ronan A, Goonewardena S, Blair JE, Hammes M, Shah D, Vasaiwala S, Kirkpatrick JN, Spencer KT : Handcarried ultrasound measurement of the inferior vena cava for assessment of intravascular volume status in the outpatient hemodialysis clinic. *Clin J Am Soc Nephrol* 1 : 749-753, 2006