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Brief Report

Comparison of Left Ventricular Diastolic Function Parameters between Patients with Unplanned and Planned Hemodialysis Initiation: A Cross-Sectional Study

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Abstract: Despite the increasing number of dialysis patients, there is still no clear consensus regarding when a permanent access device should be prepared and renal replacement treatment should be undertaken. The purpose of this study was to evaluate left ventricular diastolic function at the start of dialysis between patients in a planned or unplanned manner according to the 2016 recommendations of the American Society of Echocardiography/European Association of Cardiovascular Imaging (ASE/EACVI). We designed a single-center, cross-sectional study to use echocardiography to evaluate and compare left ventricular diastolic function at the onset of dialysis between patients in planned and unplanned groups. A total of 21 patients were included in our analysis (11 initiated dialysis in a planned manner and 10 did so in an unplanned manner). E/A and E/E′ were significantly high in the unplanned dialysis initiation group ($p = 0.048$ and $p = 0.003$, respectively). Furthermore, the number of patients with an E/E′ ratio of >14 and tricuspid regurgitation velocity of >2.8 was also significantly high in the unplanned dialysis initiation group (80% vs. 18%; $p = 0.009$, 40% vs. 0%; $p = 0.035$, respectively). According to the American Society of Echocardiography and the European Association of Cardiovascular Imaging Recommendation in 2016, the number of patients with left ventricular diastolic dysfunction was significantly high in the unplanned dialysis initiation group (80% vs. 18%; $p = 0.009$). The current study demonstrated that left ventricular diastolic dysfunction is more apparent in incident dialysis patients in an unplanned manner. Our findings suggest that the assessment of left ventricular diastolic function by echocardiography may be an indication of when to create a permanent access device and initiate dialysis.

Keywords: kidney failure; hemodialysis; ventricular dysfunction; echocardiography

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1. Introduction

In Japan at the end of 2021, the number of dialysis patients exceeded 340,000, and more than 40,000 individuals with end-stage kidney disease (ESKD) initiated maintenance dialysis in 2021. Clinical guidelines recommend the planned use of arteriovenous access (arteriovenous fistula or graft) rather than the unplanned use of a central venous catheter (CVC) in incident dialysis patients because unplanned dialysis initiation is associated with increased patient morbidity, mortality, and health care costs [1–6]. However, many patients with ESKD begin dialysis in an unplanned manner. It is estimated that approximately 40–70% of patients initiate dialysis in this manner, despite nephrologists' care [7–10]. The common risk factors associated with unplanned dialysis initiation are increased age, lower estimated glomerular filtration rate (eGFR) at dialysis initiation, and the presence of cardiovascular disease, congestive heart failure, and diabetes mellitus [9,11,12]. These

factors are common in patients with ESKD and are not specific for predicting or preventing unplanned dialysis initiation.

Left ventricular diastolic dysfunction (LVDD) is associated with heart failure, cardiovascular events, and high mortality in patients with chronic kidney disease (CKD) and ESKD [13–18]. Furthermore, a recent study showed that LVDD is predictive of cardiovascular events in 'incident dialysis patients' [19]. However, the potential association between LVDD and dialysis initiation has not been investigated.

The purpose of this study was to evaluate left ventricular (LV) diastolic function at the start of dialysis between patients in a planned or unplanned manner according to the 2016 recommendations of the American Society of Echocardiography/European Association of Cardiovascular Imaging (ASE/EACVI) [20].

2. Materials and Methods

2.1. Study Design and Population

This was a cross-sectional, single-center study. From April 2020 to March 2022, 21 patients were assessed using echocardiography (10 patients in unplanned dialysis initiation and 11 patients who began dialysis in a planned manner). The exclusion criteria were as follows: (i) atrial fibrillation, (ii) mitral stenosis, (iii) mitral annular calcification, and (iv) left bundle branch block. 3 patients with atrial fibrillation and 2 patients with mitral annular calcification were excluded. 3 patients did not consent to participate in this study. An unplanned dialysis initiation is defined as dialysis initiation with a CVC when vascular access is not ready for use or requires hospitalization. We referred to the methods of Mendelssohn et al., 2009 and Christopher et al., 2019 [3,21]. All patients were initiated on hemodialysis.

2.2. Data Collection

Demographic data and clinical characteristics, including age, sex, body mass index (BMI), blood pressure, referral to nephrologists, co-morbidities, medications, and reasons for dialysis initiation were recorded at dialysis initiation. The following laboratory data were measured using blood samples collected immediately before hemodialysis initiation: levels of urea nitrogen, creatinine, eGFR, sodium, potassium, calcium, phosphorus, hemoglobin, hematocrit, ferritin, albumin, fasting glucose, fasting low-density lipoprotein, and fasting triglyceride. The clinical indications of dialysis initiation were shown as uremic symptoms (increasing fatigue, appetite loss, and nausea/vomiting), volume overload, and others (hyperkalemia, increased creatinine).

2.3. Echocardiography

Echocardiography was performed within the 24 h preceding the start of dialysis. Echocardiographic measurements were performed using a standard cardiac ultrasound device (Aplio a400 or Aplio i700, Canon Medical Systems Corporation, Tochigi, Japan). Patient information was blinded. All images were obtained by M-mode, two-dimensional, and Doppler measurements according to the 2016 ASE/EACVI recommendations [20]. LV systolic function was measured by the LV ejection fraction (LVEF), which was obtained using the biplane modified Simpson method of discs from apical four- and two-chamber views. The early filling velocity (E wave), atrial contraction velocity (A wave), and E/A ratio were measured using mitral transvalvular flow in a four-chamber apical view. Tissue Doppler velocities were measured in a four-chamber apical view. The early diastolic mitral annular velocities (E′ wave) were measured by the junction of the LV lateral and septal walls, and the E/E′ ratio was calculated. Left atrial (LA) volume was measured using Simpson's biplane method by the apical two- and four-chamber views. The left atrial volume index (LAVI) was calculated by the body surface area. The 2016 recommendations of the ASE/EACVI defined LV diastolic function by four variables. The four recommended variables and their abnormal cutoff values are annular E′ velocity (septal E′ < 7 cm/s, lateral E′ < 10 cm/s), average E/E′ ratio > 14, LAVI > 34 mL/m^2, and peak TR velocity > 2.8 m/s.

LV diastolic function is normal if more than half of the available variables do not meet the cutoff values for identifying abnormal function. LVDD is present if more than half of the available parameters meet these cutoff values [20].

2.4. Statistical Analysis

The Shapiro–Wilk test of normality was used for the data distribution analysis. No continuous variables were normally distributed; they are presented as the median (interquartile range) and compared using the Mann–Whitney U test between the planned and unplanned dialysis initiation groups. Categorical variables are presented as absolute numbers (percentages) and were compared using Fisher's exact test. Statistical significance was set at $p < 0.05$. All statistical analyses were performed using EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan) [22].

3. Results

3.1. Patient Characteristics

Table 1 lists the clinical characteristics of the study participants. The groups did not differ in terms of the participants' age, sex, BMI, blood pressure, referral to nephrologists, or the prevalence of hypertension, dyslipidemia, diabetes, hyperuricemia, and cardiovascular disease. Compared with patients in the planned dialysis initiation group (planned group), patients in the unplanned dialysis initiation group (unplanned group) were more likely to use a renin–angiotensin system inhibitor (80% vs. 18%; $p = 0.009$) and less likely to use an erythropoiesis-stimulating agent (30% vs. 91%; $p = 0.008$). No significant difference was observed in the number of patients with uremic symptoms or volume overload between the two groups in terms of the reasons for dialysis initiation. Table 2 lists the hematological and biochemical results. The serum albumin level of the unplanned group was significantly lower than that of the planned group (2.7 (2.3–3.4) g/dL vs. 3.3 (3.1–3.7) g/dL; $p = 0.006$). No differences were observed between the two groups for the other data.

3.2. Echocardiography

The echocardiographic parameters are listed in Table 3. The two groups did not significantly differ in terms of LA diameter, LAVI, LV size, LVEF, A wave velocity, deceleration time, and TRV. The E and E′ wave velocities were higher and lower in the unplanned and planned groups, respectively, although the difference was not significant. The E/A and E/E′ ratios were significantly higher in the unplanned group than in the planned group ($p = 0.048$ and $p = 0.003$, respectively). In both groups, most patients had preserved LVEF. Table 4 lists the echocardiographic parameters used to evaluate the LV diastolic function. The number of patients with an E/E′ ratio of >14 and TRV of >2.8 was significantly higher in the unplanned group (80% vs. 18%; $p = 0.009$, 40% vs. 0%; $p = 0.035$, respectively) than in the planned group. According to the 2016 ASE/EACVI algorithm, the number of patients with LVDD was significantly higher in the unplanned group than in the planned group (80% vs. 18%; $p = 0.009$).

Table 1. Clinical characteristics.

Variables	Planned (n = 11)	Unplanned (n = 10)	p-Value
Age, years	74 (72–79)	75 (66–77)	0.75
Male sex (%)	9 (82)	6 (60)	0.36
BMI, kg/m^2	21.5 (20.7–22.5)	24.1 (21.6–26.4)	0.15
SBP, mmHg	150 (143–158)	145 (131–165)	0.78
DBP mmHg	81 (70–92)	70 (60–80)	0.16
Referral to nephrologists (%)	7 (64)	7 (70)	1.0
Comorbidities			
Hypertension (%)	10 (91)	10 (100)	1.0
Dyslipidemia (%)	9 (82)	5 (50)	0.18

Table 1. *Cont.*

Variables	Planned (n = 11)	Unplanned (n = 10)	p-Value
Diabetes (%)	7 (64)	5 (50)	0.67
Hyperuricemia (%)	10 (91)	7 (70)	0.31
CVD (%)	2 (18)	5 (50)	0.18
Medications			
ACEI/ARB (%)	2 (18)	8 (80)	0.009
β-blocker (%)	3 (27)	7 (70)	0.086
CCB (%)	10 (91)	9 (90)	1.0
Diuretics (%)	4 (36)	7 (70)	0.2
Statin (%)	9 (82)	4 (40)	0.081
ESA (%)	10 (91)	3 (30)	0.008
Reasons for commencing dialysis			
Uremic symptom (%)	5 (45)	4 (40)	1.0
Volume overload (%)	3 (27)	4 (40)	0.66
Other (%)	3 (27)	2 (20)	1.0

SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; CVD, Cardiovascular diseases; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; CCB, calcium channel blocker; ESA, erythropoiesis-stimulating agent.

Table 2. Hematological and biochemical characteristics.

Variables	Planned (n = 11)	Unplanned (n = 10)	p-Value
Serum urea nitrogen, mg/dL	77.7 (55.2–94.6)	73.4 (64.5–78.3)	0.92
Serum creatinine, mg/dL	7.0 (5.9–8.0)	6.7 (5.8–9.2)	0.97
eGFR, mL/min per 1.73 m^2	6.5 (5.6–7.6)	7.3 (4.0–8.3)	1.0
Serum sodium, mEq/L	140 (139–142)	139 (137–141)	0.30
Serum potassium, mEq/L	4.4 (4.2–5.0)	4.1 (3.9–4.5)	0.23
Serum calcium, mg/dL	8.9 (8.7–9.6)	9.1 (8.9–9.9)	0.48
Serum phosphate, mg/dL	4.9 (4.7–5.7)	5.4 (4.9–6.3)	0.42
Hemoglobin, g/L	9.3 (8.8–10.5)	9.0 (7.6–10.1)	0.60
Hematocrit, %	28.9 (26.9–32.4)	27.7 (23.3–30.6)	0.48
Serum Ferritin, ng/mL	94.7 (72.5–122.2)	127.3 (41.9–194.8)	0.89
Serum albumin, g/dL	3.3 (3.1–3.7)	2.7 (2.3–3.4)	0.006
Fasting glucose, mg/dL	102 (96–121)	108 (103–135)	0.26
Fasting LDL cholesterol, mg/dL	73 (58–78)	79 (70–133)	0.26
Fasting triglyceride, mg/dL	141 (108–153)	103 (66–154)	0.53

eGFR, estimated glomerular filtration rate; LDL, low density lipoprotein.

Table 3. Echocardiographic parameters.

Variables	Planned (n = 11)	Unplanned (n = 10)	p-Value
LAD (mm)	37.0 (34.1–40.8)	40.3 (38.5–45.6)	0.34
LAVI (mL/m^2)	44.7 (38.2–53.1)	51.1 (46.8–59.8)	0.25
LVEDD (mm)	50.0 (49.2–52.5)	49.6 (45.6–54.5)	0.67
LVESD (mm)	32.0 (30.2–35.8)	35.2 (29.7–37.2)	0.60
LVEF (%)	65.0 (62.0–68.4)	60.1 (56.3–64.6)	0.18
LVEF $\geq$ 50 (%)	10 (91)	8 (80)	0.59
E (cm/s)	78.7 (63.5–94.5)	110.5 (84.0–121.7)	0.051
A (cm/s)	110.6 (93.6–120.3)	94.4 (73.9–109.8)	0.25
E/A	0.86 (0.71–0.90)	1.20 (0.81–1.80)	0.048
DT (msec)	200 (177–223)	192 (176–227)	0.94
E′ (cm/s)	7.5 (6.1–9.0)	6.3 (5.5–6.4)	0.07
E/E′	10.4 (9.5–12.8)	17.6 (15.0–18.5)	0.003
TRV (m/s)	2.41 (2.23–2.49)	2.65 (2.23–3.08)	0.16

LAD, left atrial diameter; LAVI, left atrial volume index; LVEDD, left ventricular end diastolic diameter; LVESD, left ventricular end systolic diameter; LVEF, left ventricular ejection fraction; E, early transmitral peak velocity; A, late transmitral peak velocity; DT, deceleration time; E′, mitral annular early diastolic peak velocity; TRV, tricuspid regurgitant velocity.

Table 4. Echocardiographic parameters for evaluating left ventricular diastolic function.

Variables	Planned (n = 11)	Unplanned (n = 10)	p-Value
LAVI > 34 (%)	9 (82)	9 (90)	1.0
E′ < 7 (%)	4 (36)	8 (80)	0.081
E/E′ > 14 (%)	2 (18)	8 (80)	0.009
TRV > 2.8 (%)	0 (0)	4 (40)	0.035
Diastolic function			
Normal (%)	7 (64)	0 (0)	
Indeterminate (%)	2 (18)	2 (20)	
Diastolic dysfunction (%)	2 (18)	8 (80)	0.009

LAVI, left atrial volume index; E, early transmitral peak velocity; E′, mitral annular early diastolic peak velocity; TRV, tricuspid regurgitant velocity.

4. Discussion

To the best of our knowledge, this cross-sectional study is the first to conduct a comparative evaluation of LV diastolic function just before dialysis initiation between patients who begin dialysis in a planned or unplanned manner according to the 2016 ASE/EACVI recommendations. The present study demonstrated that LVDD and elevated estimated LV diastolic filling pressure are more apparent in incident dialysis patients who begin treatment in an unplanned manner.

LVDD results from impaired LV relaxation and increased LV chamber stiffness, which increases cardiac filling pressures. The 2016 ASE/EACVI recommendations first used this method to detect LVDD, and then evaluate the degree of LV filling pressure elevation to assess the severity of LVDD. LVDD is always present in patients with a reduced LVEF [20]. LVDD is a cardiovascular abnormality frequently detected in patients with CKD, and advanced CKD is independently predictive of progressive LVDD [14,16,23]. Furthermore, several studies have found that the prevalence of LVDD increases with age and with the presence of cardiovascular co-morbidities [24,25]. In the present study, there was no significant difference between the two groups in terms of eGFR, age, or cardiovascular co-morbidities. However, the number of patients with LVDD was significantly higher in the unplanned group than in the planned group, although there were few patients with reduced LVEF in either group.

In the 2016 ASE/EACVI recommendations, the left ventricular filling pressure was estimated using the E/A ratio, the E′ wave velocity, the E/E′ ratio, LAVI, and TRV. In the current study, the E/A and E/E′ ratios were significantly higher in the unplanned group than in the planned group. The E′ wave velocity and LAVI were not significantly different between the two groups. However, most patients across both groups had LAVI > 34 mL/m^2, which is an index of elevated left ventricular filling pressure. LA volume is an accurate measure of LA size [26]. With increased stiffness of the left ventricle, LA pressure rises to maintain adequate LV filling, and chronic increased atrial wall tension leads to chamber dilatation and atrial remodeling [27]. Increased LAVI often reflects the cumulative effect of filling pressure over time, while the Pulse Doppler parameters only provide information about LV filling at the time of measurement [28,29]. In our study, the atrial remodeling from chronic pressure overload progressed in both groups, although LV filling pressure was significantly elevated in the unplanned group. This resulted in a significantly higher number of patients with LVDD in the unplanned group, according to the 2016 ASE/EACVI guidelines [20]. These results in the unplanned group may be more significantly affected by sudden volume overload, such as flash pulmonary edema. However, there was no significant difference between the two groups of patients in terms of volume overload being the reason for dialysis initiation. Furthermore, in the present study, both the E/E′ ratio and the number of patients with E/E′ > 14, an index of elevated LV filling pressure, were significantly higher in the unplanned group than in the planned group. Previous studies have suggested that E′ is relatively unaffected by the patient's volume status; the E/E′ ratio is a practicable and reproducible index to assess the LV filling pressure, and an elevated E/E′ ratio is a parameter that reflects LV relaxation and stiffness [30–32]. Therefore, in our

study, the number of patients with LVDD was significantly higher in the unplanned group than in the planned group.

Despite the increasing number of patients with CKD and on dialysis, there is still no clear consensus on when a permanent access device should be prepared and renal replacement treatment should be undertaken [1,21,33–38]. Previous studies have found that unplanned dialysis initiation is associated with increased patient morbidity, mortality, and health care costs [1–6]. The common risk factors for unplanned dialysis initiation are increased age, lower estimated glomerular filtration rate (eGFR) at dialysis initiation, and the presence of cardiovascular disease, congestive heart failure, and diabetes mellitus [9,11,12]. However, these factors are common in patients with ESKD and the lack clinical specificity that can help to predict and prevent unplanned dialysis initiation. Unfortunately, we could not perform a multivariate analysis because the sample size was not sufficiently large. Our study had other limitations. First, this was a single-center study. Second, the study design was observational in nature. Third, we could not perform multivariate analysis owing to the small sample size of this study. Fourth, the patients in this study were only ethnic Japanese. Finally, we did not assess quantitative body fluid status. However, our results suggest that the assessment of LV diastolic function by echocardiography may indicate when to create a permanent access device and initiate dialysis. We believe that our results will contribute to preventing unplanned dialysis initiation. Larger prospective multicenter studies are required to fully understand this association.

5. Conclusions

We evaluated LV diastolic function just before dialysis initiation between patients who commenced treatment in a planned and unplanned manner, according to the 2016 ASE/EACVI recommendations. This study demonstrated that LVDD and elevated estimated LV diastolic filling pressure are more apparent in incident dialysis patients who commence dialysis in an unplanned manner. Although the current study has some limitations, our results indicate that the assessment of LV diastolic function by echocardiography may indicate when to create a permanent access device and initiate dialysis. We believe that echocardiographic information should be used more effectively in patients with ESKD before the dialysis initiation.

Author Contributions: T.Y. designed the study. T.Y., M.S. and N.I. collected, entered, and analyzed the data. S.I., H.K. and Y.H. performed the data collection. All authors have read and agreed to the published version of the manuscript.

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Informed Consent Statement: Written informed consent was obtained from each patient prior to their participation in the study.

Data Availability Statement: The data are available and will be shared upon reasonable request by the corresponding author. However, they are not public due to ethical and regulatory issues.

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