Prevalence and Factors Associated with Left Ventricular Systolic Dysfunction in End-Stage Renal Disease Patients on Dialysis

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Background: *Heart failure is a major cause of morbidity and mortality in patients with end-stage renal disease (ESRD). Previous studies reported various factors associated with left ventricular systolic dysfunction (LVSD) in patients with ESRD.*
Objective: *To investigate the prevalence and factors associated with LVSD in patients with ESRD on dialysis.*
Material and Method: *Patients with ESRD on dialysis who underwent comprehensive transthoracic echocardiography at Siriraj Hospital between 2003 and 2014 were enrolled. LVSD was defined as left ventricular ejection fraction less than 40%.*
Results: *One hundred sixty one patients with a mean age of 56.5±15.4 years were included and 46% were female. Regarding mode of dialysis, 25% and 75% of patients were on peritoneal dialysis and hemodialysis, respectively. Median duration of dialysis was three years. Smoking, diabetes, dyslipidemia, and hypertension were reported in 30%, 40%, 57%, and 94% of patients, respectively. History of heart failure and coronary artery disease (CAD) were reported in 23% and 24% of cases, respectively. Prevalence of LVSD was 5%. History of heart failure, known CAD, and left ventricular diastolic dimension (LVDd) were found to be univariately associated with LVSD. Multivariate factors associated with LVSD were known CAD (OR 23.67, 95% CI 1.23-456.54, p-value = 0.036) and LVDd (OR 1.56, 95% CI 1.15-2.11, p-value = 0.004).*
Conclusion: *Prevalence of LVSD in patients with ESRD on dialysis in the present study was 5%. Known CAD and LVDd were independent predictors of LVSD in this population.*

Keywords: *Dialysis, End-stage renal disease, Left ventricular systolic dysfunction, Heart failure*

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Cardiovascular diseases are a leading cause of morbidity and mortality in patients with end-stage renal disease (ESRD), and they manifest variously as acute myocardial infarction, cerebrovascular events, heart failure, sustained arrhythmia, or sudden cardiac death[1-5]. Of these various manifestations, heart failure is common[5]. Patients may present with either systolic heart failure (systolic dysfunction) or diastolic heart failure (diastolic dysfunction). Advanced age, pre-existing heart disease (left ventricular systolic dysfunction [LVSD], ischemic heart disease), and chronic uremia have been suggested as important risk factors for heart failure in hemodialysis patients[5-8]. Previous studies reported factors associated with LVSD in patients with ESRD, including age, hypertension, anemia, serum albumin, pulse pressure, pulse rate, and chronic cardiovascular disease[6,7,9,10]. Adjusted for other risk factors, LVSD is strongly associated with mortality. In recent studies, LVSD was found in 4.7 to 48% of patients with ESRD[3,5,7-10]. Patients with LVSD may be symptomatic or asymptomatic. Even in asymptomatic patients, LVSD portends poor prognosis. Prevalence rates of LVSD in patients with ESRD vary due to characteristic differences among study populations and the use of different cut-off values. Since LVSD is associated with poor prognosis and proper therapy provides benefit in improving symptoms and prognosis, screening with echocardiography should be recommended in patients with ESRD. Data regarding LVSD in Thai dialysis patients are limited. The authors, therefore, aimed to study prevalence and factors associated with LVSD in Thai dialysis patients at Siriraj Hospital.

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Material and Method

Study population

This retrospective cohort study reviewed cases of 161 ESRD patients on dialysis who received treatment at Siriraj Hospital between 2003 and 2014.

The present study protocol was approved by the Siriraj Institutional Review Board. The permission of data retrieval was granted from the director of the hospital. Inclusion criteria were patients aged 18 to 80 years with ESRD on dialysis treatment (hemodialysis [HD] or peritoneal dialysis [PD]) who underwent a comprehensive transthoracic echocardiography for clinical indications at Siriraj Hospital. Exclusion criteria were poor-quality echocardiographic images, incomplete clinical or echocardiographic data, and patients diagnosed with one or more of the following: moderate to severe left-sided valvular disease, congenital heart disease, history of valve surgery, or myocardial disease. Patient demographic and clinical data were retrieved from medical records, including outpatient department record form, dialysis unit record form, echocardiographic database, and online electronic data. Patients provided written informed consent after being briefed on the objectives and protocol of the study. Clinical and echocardiographic data were recorded, including baseline characteristics (age, gender, cardiovascular risk factors, and comorbidities), indications for dialysis, duration of renal disease, mode, duration and frequency of dialysis, presence of symptoms (dyspnea, leg edema), current medications, blood chemistry, and electrocardiographic and echocardiographic findings.

Each participant was scheduled for a comprehensive transthoracic echocardiographic examination. Echocardiographic parameters were measured on three consecutive cardiac cycles and the average was used for statistical analysis. Echocardiographic examination consists of two-dimensional, M-mode, conventional Doppler, and tissue Doppler imaging measurements. Left ventricular systolic function was measured by modified Simpson's method. LVSD was defined as left ventricular ejection fraction less than 40%. Patients with LVSD were prescribed further treatment.

Statistical analysis

Baseline characteristics were described using descriptive statistics, including frequency and percentage for categorical variables. Continuous variables were reported as mean ± standard deviation for normally distributed variables and median (minimum and maximum) for non-normally distributed variables. Normality of distribution of variables was examined by Kolmogorov-Smirnov test. Prevalence of LVSD was described as percentage and 95% confidence interval (CI). Association of continuous variables with LVSD was determined using Student's t-test or Mann-Whitney U test. For categorical variables, Chi-square test or Fisher's exact test was used. Variables found to be significantly associated with LVSD in univariate analysis were further evaluated in multivariate analysis using multiple logistic regression in backward stepwise method and presented as odds ratio, included 95% CI. For all tests performed, a two-tailed p-value <0.05 was considered to be statistically significant. All statistical analyses were performed using SPSS software version 18.0 (SPSS, Inc., Chicago, IL, USA).

Results

Of the 241 participants obtained from the patient list of Siriraj Dialysis Unit, 161 patients underwent comprehensive transthoracic echocardiographic examination and were included in this study. Patient baseline characteristics are shown in Table 1. Mean age was 56.5±15.4 years and 46% of patients were female. Regarding mode of dialysis, 25% and 75% of patients were on PD and HD, respectively. Median duration of dialysis was three years. Smoking, diabetes mellitus, dyslipidemia, and hypertension were reported in 30%, 40%, 57%, and 94% of patients, respectively. History of transient ischemic attack or stroke, heart

Table 1. Clinical characteristics of study population

Variables	n = 161
Age (years)	56.5±15.4
Body mass index (kg/m^2)	23.0±4.3
Dyspnea	53 (34)
Edema	36 (23)
Hypertension	150 (94)
Diabetes mellitus	61 (40)
Dyslipidemia	92 (57)
Smoking	17 (30)
Family history of premature CAD	8 (16)
Medication use	
Calcium channel blockers	99 (64)
Beta blockers	91 (60)
Statins	86 (56)
Diuretics	75 (48)
Antiplatelets	64 (42)
ACEI/ARB	63 (40)
Alpha-blockers	42 (27)
Vasodilators	40 (26)
Nitrates	34 (22)

ACEI/ARB = angiotensin converting enzyme inhibitor/ angiotensin receptor blocker; CAD = coronary artery disease
Data are expressed as mean ± standard deviation or frequency (%)

failure, and known CAD was reported in 10%, 23%, and 24% of cases, respectively. Primary indications for echocardiography were preoperative evaluation before non-cardiac surgery (including kidney transplant) (46%) and presence of symptoms (35%).

Prevalence and factors associated with LVSD in dialysis patients

LVSD was reported in eight patients, three in HD group, and five in PD group. Prevalence of LVSD was 5% (95% CI 2.2-9.6%). Regarding baseline characteristics, there was no statistically significant difference in cardiovascular risk factors, comorbidities, indications for echocardiography, or modes of dialysis between patients with or without LVSD (*p*-value >0.05). History of heart failure and known CAD were significantly more prevalent in patients with LVSD (Table 2). Calcium channel blockers were more commonly used in patients without LVSD (*p*-value = 0.026). History of heart failure, known CAD, presence of Q wave on electrocardiogram, and left ventricular diastolic dimension (LVDd) were univariately associated with LVSD. Variables associated with LVSD in multivariate analysis were known CAD (OR 23.67, 95% CI 1.23-456.54, *p*-value = 0.036) and LVDd (OR 1.56, 95% CI 1.15-2.11, *p*-value = 0.004) (Table 3).

Table 2. Clinical characteristics of the study population according the group of left ventricular systolic function

Variables	LVEF ≥40% (n = 153)	LVEF <40% (n = 8)	*p*-value
Age (year)	56.0±15.3	61.8±17.8	0.313
Gender	78 (52.0)	7 (87.5)	0.069
Body mass index	23.0±4.2	23.0±6.2	0.975
Hemodialysis	117 (76.5)	3 (37.5)	0.102
Symptomatic patients	52 (34.0)	4 (50.0)	0.089
Dyspnea	50 (32.7)	3 (37.5)	0.831
Hypertension	142 (93.0)	8 (100)	1.0
Diabetes mellitus	58 (38.0)	3 (37.5)	1.0
Dyslipidemia	87 (57.0)	5 (62.5)	1.0
Smoking	15 (10.0)	2 (67.0)	0.191
Family history of premature CAD	6 (4.0)	2 (67.0)	0.065
Prior TIA	15 (10.0)	0	1.0
History of heart failure	32 (21.0)	5 (62.5)	0.017
History of CAD	32 (21.0)	6 (75.0)	0.002

CAD = coronary artery disease; LVEF = left ventricular ejection fraction; TIA = transient ischemic attack
Data are expressed as mean ± standard deviation or frequency (%)

Discussion

The present study evaluated prevalence and factors associated with LVSD in ERSD patients on dialysis at Siriraj Hospital in Bangkok, Thailand. The study population represented dialysis patients in an outpatient setting, including symptomatic and asymptomatic patients on PD or HD having any duration of renal disease. Prevalence of LVSD in the present study was 5%. Known CAD and LVDd were found to be independent parameters associated with LVSD.

Prevalence of LVSD in this study was lower than rates reported from previous studies[3,5,7-10]. Possible explanations include differences in study populations (e.g., geographical region, ethnicity, duration of ESRD, and number of subjects with history of heart failure, CAD, and/or comorbidities), definition of LVSD, and method/criteria used to determine LVSD. In addition, the selection bias might affect the prevalence of the disease. The patients who underwent transthoracic echocardiography might have multiple cardiovascular risks or were subjected to cardiovascular problems, which might affect the prevalence of

Table 3. Univariate and multivariate factors associated with left ventricular systolic dysfunction in dialysis patients

Variables	Univariate odds ratio (95% CI)	*p*-value	Multivariate odds ratio (95% CI)	*p*-value
History of heart failure	6.25 (1.42-27.55)	0.015	-	-
Known CAD	11.34 (2.19-58.89)	0.004	23.67 (1.23-456.54)	0.036
ECG (QRS duration)	1.02 (0.99-1.06)	0.207	-	-
ECG (Q wave)	11.23 (2.16-58.37)	0.003	-	-
LVDd	1.35 (1.15-1.60)	<0.001	1.56 (1.15-2.11)	0.004
IVSd	0.82 (0.61-1.10)	0.177	-	-
Serum albumin	0.34 (0.11-1.06)	0.063	-	-

CAD = coronary artery disease; CI = confidence interval; ECG = electrocardiography; IVSd = interventricular septal thickness during diastole; LVDd = left ventricular diastolic dimension

LVSD. The pre-operative group (e.g., pre-kidney transplantation) who might had better systolic function was also included. The importance of LVSD in dialysis patients has been emphasized in previous studies[3,5,7,10]. Increased mortality was reported in dialysis and post-transplantation populations who had overt heart failure[13,14]. Presence of LVSD in ESRD patients on dialysis is a reliable predictor of those at higher risk of cardiovascular events. This study demonstrated that known CAD and LVDd are independent factors associated with LVSD. Further studies are needed to clarify the mechanisms of and therapeutic options for LVSD in dialysis patients. Kidney transplantation is the ultimate therapeutic strategy for patients with ESRD, with improvement in left ventricular systolic function expected within two to three years after engraftment[15,16].

The strength of the present study centers on this being the first study to assess echocardiographic parameters as factors associating with LVSD in ESRD patients on dialysis in Thailand. Information regarding prevalence of LVSD in dialysis patients is of clinical importance from an epidemiological perspective. Limitations of this study include the relatively small sample size and the retrospective study design, which might have a selection bias effect on the results. However, all of the risk factors and indications for echocardiogram were adjusted for association analysis.

Conclusion

Prevalence of LVSD in patients with ESRD on dialysis in this study was 5%. Known CAD and LVDd were independent predictors of LVSD in this population.

What is already known on this topic?

Previous studies have reported prevalence and importance of LVSD in patients with ESRD, although cutoff values vary by study and among study populations. LVSD is a strong predictor of heart failure and mortality in patients with ESRD. Several factors have been found to associate with LVSD in patients with ESRD, including age, hypertension, anemia, serum albumin, pulse pressure, pulse rate, and chronic cardiovascular disease.

What this study adds?

Data regarding prevalence and significance of LVSD in dialysis patients among Thai population are limited. This is the first study to report prevalence and factors associated with LVSD in patients with ESRD on dialysis in Thailand. This study also presents information from an epidemiological perspective that may be useful in the development of health care policy and prevention strategy.

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Potential conflicts of interest

None.

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ความชุกของภาวะหัวใจห้องล่างซ้ายบีบตัวลดลงในผู้ป่วยภาวะไตวายขั้นสุดท้ายที่รักษาด้วยการล้างไต

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ภูมิหลัง: *ภาวะหัวใจล้มเหลวเป็นสาเหตุหลักของความทุพพลภาพและการเสียชีวิตในผู้ป่วยภาวะไตวายขั้นสุดท้าย ที่ได้รับการรักษาด้วยการล้างไต ซึ่งจากการศึกษาก่อนหน้านี้ พบว่ามีปัจจัยหลายอย่างที่มีความสัมพันธ์กับภาวะหัวใจห้องล่างซ้ายบีบตัวลดลงในผู้ป่วยกลุ่มนี้*

วัตถุประสงค์: *ศึกษาถึงความชุกและปัจจัยที่มีความสัมพันธ์กับภาวะหัวใจห้องล่างซ้ายบีบตัวลดลงในผู้ป่วยไตวายขั้นสุดท้ายที่ได้รับการรักษาด้วยการล้างไต*

วัสดุและวิธีการ: *ผู้ได้รับการคัดเลือกเข้าร่วมการศึกษา ได้แก่ ผู้ป่วยภาวะไตวายขั้นสุดท้ายที่รักษาด้วยการล้างไตที่ได้รับการตรวจคลื่นเสียงสะท้อนหัวใจผ่านทางหน้าอกที่โรงพยาบาลศิริราช ผลการตรวจพบการบีบตัวของหัวใจห้องล่างซ้ายน้อยกว่าร้อยละ 40 จะได้รับการวินิจฉัยว่ามีภาวะหัวใจห้องล่างซ้ายบีบตัวลดลง*

ผลการศึกษา: *ผู้เข้าร่วมการศึกษาทั้งหมด 161 ราย อายุเฉลี่ย 56.5±15.4 ปี เป็นเพศหญิงร้อยละ 46 อัตราผู้ที่ได้รับการล้างไตทางหน้าท้องร้อยละ 25 และการฟอกเลือดร้อยละ 75 ค่ามัธยฐานของระยะการล้างไตคือ 3 ปี จากการศึกษาพบว่าผู้เข้าร่วมการศึกษาที่มีปัจจัยเสี่ยงในเรื่องการสูบบุหรี่จำนวนร้อยละ 30 โรคเบาหวานร้อยละ 40 ภาวะไขมันในโลหิตสูงร้อยละ 57 และโรคความดันโลหิตสูงร้อยละ 94 ผู้เข้าร่วมการศึกษามีประวัติเรื่องภาวะหัวใจล้มเหลวร้อยละ 23 และได้รับการวินิจฉัยโรคหลอดเลือดแดงโคโรนารีร้อยละ 24 ความชุกของภาวะหัวใจห้องล่างซ้ายบีบตัวลดลงในผู้ป่วยไตวายขั้นสุดท้ายที่ได้รับการรักษาด้วยการล้างไตเท่ากับร้อยละ 5 การวิเคราะห์ตัวแปรตัวเดียวพบว่า ปัจจัยที่มีความสัมพันธ์กับภาวะหัวใจห้องล่างซ้ายบีบตัวลดลงอย่างมีนัยสำคัญทางสถิติได้แก่ ประวัติภาวะหัวใจล้มเหลวโรคหลอดเลือดแดงโคโรนารี และค่าขนาดของหัวใจห้องล่างซ้ายขณะคลายตัวจากการตรวจคลื่นเสียงสะท้อนหัวใจ การวิเคราะห์หลายตัวแปรพบว่าปัจจัยที่มีความสัมพันธ์กับภาวะหัวใจห้องล่างซ้ายบีบตัวลดลง ได้แก่ โรคหลอดเลือดแดงโคโรนารี (ค่า odd ratio เท่ากับ 23.67 ช่วงความเชื่อมั่นร้อยละ 95 คือ 1.23-456.54, p-value = 0.036) และค่าขนาดของหัวใจห้องล่างซ้ายขณะคลายตัวจากการตรวจคลื่นเสียงสะท้อนหัวใจ (ค่า odd ratio เท่ากับ 1.56 ช่วงความเชื่อมั่นร้อยละ 95 คือ 1.15-2.11, p-value = 0.004)*

สรุป: *ความชุกของภาวะหัวใจห้องล่างซ้ายบีบตัวลดลง ในผู้ป่วยไตวายขั้นสุดท้ายที่ได้รับการรักษาด้วยการล้างไตในการศึกษานี้เท่ากับร้อยละ 5 ปัจจัยที่มีความสัมพันธ์กับภาวะหัวใจห้องล่างซ้ายบีบตัวลดลงอย่างมีนัยสำคัญทางสถิติ ได้แก่ โรคหลอดเลือดแดงโคโรนารีและค่าขนาดของหัวใจห้องล่างซ้ายขณะคลายตัวจากการตรวจคลื่นเสียงสะท้อนหัวใจ*