Original Article

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Outcomes of open heart surgery in patients with end-stage renal disease

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Background: Cardiovascular diseases of chronic dialysis patients are often undertreated because of their higher surgical risk. This study aimed to assess mortality and morbidity after open heart surgery in chronic dialysis patients compared to those with normal renal function and identify risk factors for postoperative outcomes.

Methods: We retrospectively analyzed 2,432 patients who underwent open heart surgery from 2002 to 2017 and collected data from 116 patients (38 patients on dialysis and 78 age-, sex-, and diabetes mellitus status-matched control patients with normal kidney function). We assessed comorbidities, New York Heart Association (NYHA) class, laboratory data, surgical methods, and postoperative outcomes.

Results: The dialysis group had more comorbidities, higher NYHA classes, and greater need for urgent surgeries compared to the control group. They exhibited significantly higher postoperative mortality (18.4% vs. 2.6%, $P = 0.005$) and more overall complications (65.8% vs. 25.6%, $P = 0.000$). Dialysis itself significantly increased relative risk for in-hospital mortality after adjustment. EuroSCORE II was not as useful as in the general population. Multivariate logistic regression analysis demonstrated that total (adjusted odds ratio [AOR], 10.7; $P = 0.029$) and in-hospital death risk (AOR, 14.7; $P = 0.033$), the durations of postoperative hospitalization (AOR, 4.6; $P = 0.034$), CRRT (AOR 36.8; $P = 0.004$), and ventilator use (AOR, 7.6; $P = 0.022$) were significantly increased in the dialysis group.

Conclusion: The dialysis group exhibited a higher risk for mortality and overcall complications after open heart surgery compared to the patients with normal renal function. Therefore, the benefit of surgical treatment must be balanced against potential risks.

Keywords: Cardiovascular disease, Dialysis, Renal insufficiency, Thoracic surgery

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Introduction

Cardiovascular disease (CVD) is a major cause of mortality in patients with end-stage renal disease (ESRD). According to the 2015 Korean registry, 36% of hemodialysis and 39% of peritoneal dialysis patients died of CVD [1]. The mortality risk for CVD is extremely high in patients with ESRD compared to the general population, even in young chronic dialysis patients. Cardiovascular mortality in patients with ESRD aged ≤ 25 years is comparable to patients aged 75 to 85 years with normal renal function [2].

A high incidence of diabetes mellitus, hypertension, and hyperlipidemia in patients with ESRD increases the risk of CVD [3]. However, these traditional risk factors alone cannot fully explain the increase in CVD incidence and mortality in these patients. Therefore, non-traditional risk factors must be considered. These include uremia-related risk factors such as uremic toxins, inflammation, oxidative stress, and bone mineral diseases [4]. In addition, fluid overload, infection, bio-incompatibility, and advanced glycation end-products caused by dialysis, may promote proinflammatory cytokine secretion, thereby increasing systemic inflammation and acute-phase responses [4]. In addition, valvular calcification is common in patients with ESRD, and the risk of infective endocarditis related to frequent vascular access is higher compared to the general population [3,5]. Because of these multiple risk factors for CVD in patients with ESRD, the chance of intervention or surgery for treating CVD gradually increases.

The development of renal replacement therapy has improved the survival rate of patients with ESRD. As a result, the demand for cardiac surgery has also increased [6,7]. However, since patients with ESRD generally have higher mortality after open heart surgery [8], chronic dialysis patients may have fewer opportunities for surgical treatment. Therefore, parameters are required to accurately predict postoperative outcomes in patients with ESRD.

EuroSCORE II is widely used to estimate the risk of cardiac surgery and has proven to be a good predictor in the general population [9–11]. EuroSCORE II is able to predict in-hospital death after cardiac surgery using basic patient information and previous medical history [10,11]. The scoring system includes critical preoperative factors such as history of ventricular tachycardia, ventricular fibrillation, acute kidney injury, cardiac massage, and ventilator and intra-aortic balloon pump support, as well as surgery-related risks such as the degree of urgency and thoracic aortic involvement.

Only a few studies have examined outcomes after open heart surgery in patients with ESRD in Korea. Therefore, this study assessed mortality and morbidity after open heart surgery in chronic dialysis patients compared to those in the general population and identified risk factors for postoperative outcomes.

Methods

Subjects

We collected all clinical data from adults aged ≥ 18 years who underwent open heart surgery between December 2002 and December 2017 in Kyungpook National University Hospital in Daegu, Korea. After excluding those who underwent surgery for cardiac tumors, congenital diseases, and trauma, 2,432 patients were retrospectively analyzed. Among these, we identified 38 patients with ESRD on maintenance dialysis at the time of surgery. We selected a matched control group with normal renal function to assess mortality and morbidity after open heart surgery in the dialysis group. The dialysis group included patients with ESRD undergoing hemodialysis or peritoneal dialysis for at least three months before cardiac surgery. The control group consisted of patients with an estimated glomerular filtration rate (GFR) of ≥ 60 mL/min/1.73 m^2 according to the modification of diet in renal disease GFR equation which had not been diagnosed with any renal disease. We randomly selected 78 patients after matching for age, sex, and diabetes mellitus status. This study was conducted under approval and waiver of informed consent from institutional review board of Kyungpook National University Hospital (KNUH-2018-09-001).

Data collection

We collected data on open heart surgery performed between 2002 and 2017 from the Department of Thoracic and Cardiovascular Surgery at Kyungpook National University Hospital. Baseline characteristics and comorbidities, laboratory data, surgical method, and postoperative outcomes were obtained retrospectively from the medical records, and the outcomes in the dialysis and control groups were compared.

Priority of surgery was classified into three groups. 1) Elective surgery: The medical factors indicate the need for surgery; however, the clinical situation allows for discharge from the hospital with re-admission for surgery at a later date. 2) Urgent: The medical factors require that the patient remain in the hospital before surgery. 3) Emergent: The medical factors relating to the patient's cardiac disease dictate that surgery should be performed within hours to prevent morbidity or mortality.

The type of surgery was divided into four groups including isolated valve procedures, isolated coronary artery bypass grafting (CABG), combined valve and CABG or other procedures, and aortic procedures. The EuroSCORE was calculated according to the age, sex, laboratory data, multiple risk factors, and type of surgery. Risk was classified into three levels (EuroSCORE ≤ 9%, low-to-moderate risk; EuroSCORE 9–25%, high risk; and EuroSCORE > 25%, very high risk). The postoperative outcomes included mortality, duration of hospitalization and ventilator use, and the occurrence of complications. Except for the patients lost to follow-up, mortality after discharge by December 2017 was also investigated.

Statistical analysis

Continuous variables were presented as means ± standard deviation or medians (interquartile ranges) as appropriate, and categorical variables as the percentage of the sample. Univariate analysis was performed with the χ^2 test for categorical variables and *t* tests for continuous variables to assess the statistical significance of the differences in patient characteristics between the dialysis and control groups. We used logistic regression analysis to assess the effect of dialysis on each outcome (expressed in terms of odds ratios [ORs]) after adjustment for potentially confounding variables. The potential confounders included sex, age, diabetes mellitus, hypertension, hypercholesterolemia, anemia, and infective endocarditis. Survival curves were estimated using the Kaplan–Meier method and compared using the log-rank test between the two groups. Statistical analysis was performed using SPSS statistics version 23.0 (IBM Corp., Armonk, NY, USA). A *P* value of ≤ 0.05 was considered significant.

Results

Table 1 lists the patient characteristics, comorbidities, and laboratory data for the dialysis and control groups. The dialysis and control groups were matched for age, sex, and status of diabetes mellitus. The percentage of males in the dialysis and control groups was 76.3% and 76.5%, respectively ($P = 0.936$). There were no significant differences in age (54 ± 10.7 years vs. 53.6 ± 10.4 years, $P = 0.849$) and percentage of patients aged ≥ 60 years (26.3% vs. 24.4%, $P = 0.819$). At the time of admission, the New York Heart Association (NYHA) class was assessed to determine the symptoms and degree of physical activity (NYHA II [26.3% vs. 56.4%, $P = 0.002$], NYHA III [50% vs. 29.5%, $P = 0.031$], and NYHA IV [23.7% vs. 14.1%, $P = 0.200$]).

Among the various comorbidities, hypertension (97.4% vs. 46.2%, $P = 0.000$), peripheral vascular disease (10.5% vs. 0%, $P = 0.010$), anemia (55.3% vs. 9.0%, $P = 0.000$), and endocarditis (23.7% vs. 5.1%, $P = 0.009$) were significantly higher in the dialysis group.

There were no significant differences in the incidence of diabetes mellitus, angina, previous myocardial infarction, heart failure, chronic obstructive pulmonary disease, stroke, and liver cirrhosis. The incidence of hypercholesterolemia (5.3% vs. 21.8%, $P = 0.024$) was lower in the dialysis group compared to the control group. In addition, a history of smoking, coronary angiography prior to admission, and left ventricular ejection fraction measured using echocardiography were not significantly different between the two groups. Surgical findings including cardiopulmonary bypass time, clamping of aortic time, and use of intra-aortic balloon pump also did not differ between the two groups (Table 1). EuroSCORE II showed no significant difference between the dialysis and control groups (Fig. 1).

The priority of surgery determined by the surgeon was presented in Table 2. The rate of urgent surgery (68.4% vs. 32.1%, $P = 0.000$) was significantly higher in the dialysis group, whereas the rate of elective surgery (26.3% vs. 60.3%, $P = 0.001$) was significantly higher in the control group. There was no significant difference in the rate of emergent surgery between the two groups. In addition, the type of surgical procedure did not differ between the groups (Table 2). Crude mortality rates (in-hospital and death after discharge) in both groups are shown in Table 3. In-hospital mortality rate (18.4% vs. 2.56%, $P = 0.005$) and death rate after discharge were significantly higher in the dialysis group. The causes of in-hospital death were as follows: 4 patients died of heart failure, 1 died of stroke, 1 died of brain hemorrhage, and 1 died of bleeding after surgery in the dialysis group, whereas 1 died of heart failure and 1 died of infective endocarditis in the control group. The in-hospital death rates were compared according to the type of procedure and EuroSCORE II. There were no significant differences in mortality by procedure type and the EuroSCORE II between the groups (data not shown).

Table 1. Patient characteristics

Characteristic	Dialysis group (n = 38)	Control group (n = 78)	*P* value
Sex, male	29 (76.3)	59 (75.6)	0.936
Age (yr)	54 ± 10.7	53.6 ± 10.4	0.849
Aged > 60 yr	10 (26.3)	19 (24.4)	0.819
Dialysis modality (HD/ PD)	20/9		0.082
Dialysis vintage (mo)			0.973
HD	55.4 (25.1–95.1)	–	
PD	55.8 (34.6–89.1)	–	
NYHA class			
II	10 (26.3)	44 (56.4)	0.002
III	19 (50.0)	23 (29.5)	0.031
IV	9 (23.7)	11 (14.1)	0.200
Preoperative comorbidities			
Diabetes mellitus	24 (63.2)	48 (61.5)	0.866
Hypertension	37 (97.4)	36 (46.2)	0.000
COPD	0 (0)	2 (2.6)	1.000
Hypercholesterolemia	2 (5.3)	17 (21.8)	0.024
Angina	8 (21.1)	7 (9.0)	0.082
Previous MI	8 (21.1)	6 (7.7)	0.065
Heart failure	5 (13.2)	6 (7.7)	0.500
Peripheral vascular disease	4 (10.5)	0 (0)	0.010
Stroke	6 (15.8)	7 (9.0)	0.349
Liver cirrhosis	1 (2.6)	1 (1.3)	0.550
Anemia[a]	21 (55.3)	7 (9.0)	0.000
Endocarditis	9 (23.7)	4 (5.1)	0.009
History of smoking	17 (44.7)	38 (48.7)	0.687
CAG prior to admission	19 (50.0)	40 (51.3)	0.897
LVEF classification (%)			
Compromised (< 30)	1 (2.6)	3 (3.8)	1.000
Moderate (30–50)	11 (28.9)	18 (23.1)	0.493
Normal (> 50)	26 (68.4)	57 (73.1)	0.602
Laboratory findings			
BUN (mg/dL)	51 ± 28.7	16.1 ± 5.8	0.000
Creatinine (mg/dL)	9.4 ± 5.1	0.9 ± 0.2	0.000
MDRD eGFR (mL/min/1.73 m^2)	7.5 ± 3.8	91.8 ± 29.0	0.000
Potassium (mg/dL)	4.6 ± 0.8	4.2 ± 0.4	0.022
Surgical findings			
CPB time (min)	256 (108.0–166.0)	124.5 (99.5–179.0)	0.717
Clamping of aorta time (min)	83 (64.0–94.5)	82.5 (69.0–94.8)	0.137
IABP	0	0	–
Continuous atrial fibrillation	0	1	–
Stay in ICU (d)	1 (1–1.5)	1 (1–1)	0.253

Data are presented as number (%), mean ± standard deviation, or median (interquartile range).

BUN, blood urea nitrogen; CAG, coronary angiography; COPD, chronic obstructive pulmonary disease; CPB, cardiopulmonary bypass; eGFR, estimated glomerular filtration rate; HD, hemodialysis; IABP, intra-aortic balloon pump; ICU, intensive care unit; LVEF, left ventricular ejection fraction; MDRD, modification of diet in renal disease; MI, myocardial infarction; NYHA, New York Heart Association; PD, peritoneal dialysis.

[a]Hemoglobin level of < 10 g/dL.

Deaths were investigated from the time of discharge until December 2017, except in those of follow-up loss (Table 3). The death rate after discharge was also higher (13.2% vs. 1.3%, P = 0.014) in the dialysis group (Table 3): 3 patients died of sepsis, 1 died of gastrointestinal bleeding, and 1 died of unknown causes, while 1 died of stroke in the control group. The median time to death after discharge was 64.9 months in the dialysis group and 31.3 months in the control group.

When postoperative complications were compared, pulmonary edema (26.3% vs. 3.8%, P = 0.001) and continuous renal replacement therapy (38.5% vs. 2.6%, P = 0.000) were more frequent in the dialysis group (Table 4). The hospitalization duration (days) was also longer in the dialysis group (25.8 ± 28.4 vs. 15.0 ± 6.3, P = 0.026). There were no significant differences in other complications. However, the overall complication rates (65.8% vs. 25.6%, P = 0.000) were significantly higher in the dialysis group (Table 4). The relative risk of in-hospital mortality for each comorbid condition or type of operation was assessed to confirm the association between each variable and perioperative mortality. Variables with relative risk higher than 2-fold are presented in Table 5. The relative risk was 16.8 for NYHA class IV, 10.2 for urgent surgery, 4.0 for endocarditis, 4.7 for hypertension, 7.2 for ESRD on dialysis, and 4 for a EuroSCORE II of 9% to 25%. After adjusting for variables including age, sex, hypertension, diabetes, hypercholesterolemia, endocarditis, and pe-

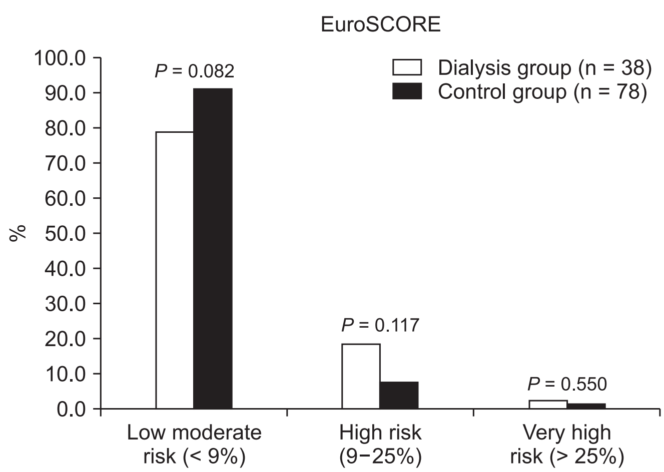

Figure 1. **EuroSCORE for the risk assessment of open heart surgery of the dialysis and control groups.**

Table 2. **Comparison of surgical procedures between groups**

Procedures	Dialysis group (n = 38)	Control group (n = 78)	*P* value
Surgery			
Elective	10 (26.3)	47 (60.3)	0.001
Urgent	26 (68.4)	25 (32.1)	0.000
Emergent	2 (5.3)	6 (7.7)	1.000
Procedure type			
Isolated valve procedure	8 (21.1)	28 (35.9)	0.105
Isolated CABG	19 (50.0)	29 (37.2)	0.188
Combined valve and CABG or other procedures	7 (18.4)	14 (17.9)	0.951
Aortic procedure	4 (10.5)	7 (9.0)	0.748

Data are presented as number (%).
CABG, coronary artery bypass grafting.
Elective indicates the need for surgery. However, the clinical situation allows discharge from the hospital with readmission for surgery at a later date. Urgent: require that the patient remain in the hospital before surgery; Emergent: based on cardiac status, surgery should be performed within hours to prevent morbidity or mortality.

Table 3. **Comparison of mortality between groups**

Mortality	Dialysis group (n = 38)	Control group (n = 78)	*P* value
Total in-hospital mortality	7 (18.4)	2 (2.6)	0.005
Causes of death (n)	Heart failure (4)	Heart failure (1)	
	Stroke (1)	Infective endocarditis (1)	
	Brain hemorrhage (1)		
	Bleeding after surgery (1)		
Total death after discharge (%)	5 (13.2)	1 (1.3)	0.014
Causes of death (n)	Sepsis (3)		
	GI bleeding (1)	Stroke (1)	
	Unknown (1)		
Duration until death after discharge (mo)	64.9 (18–99)	31.3	

Data are presented as number (%), number only, or median (interquartile range).
GI, gastrointestinal.

ripheral vascular disease, dialysis exhibited the highest relative risk for mortality.

The estimated OR for in-hospital mortality in the dialysis group relative to the control group was 14.7 (P = 0.033) after adjustment for multiple variables (Table 6). The total mortality was significantly higher in the dialysis group (adjusted OR, 10.7; P = 0.029) (Table 6), while the survival curve using the Kaplan–Meier method also exhibited a significant difference (P = 0.000) (Fig. 2). In addition, dialysis increased the risk of complications, including continuous renal replacement therapy (adjusted OR, 36.8; P = 0.004), hospitalization duration (adjusted OR, 4.6; P = 0.034), and ventilation duration (adjusted OR, 7.6; P = 0.022). In addition, the dialysis group showed a 5-fold overall higher risk for complications (adjusted OR 5.7, P = 0.006) compared to the control group.

Table 4. Postoperative complications in each group

Complications	Dialysis group (n = 38)	Control group (n = 78)	*P* value
Pulmonary edema	10 (26.3)	3 (3.8)	0.001
Pneumonia	3 (7.9)	10 (12.8)	0.541
Sepsis	3 (7.9)	3 (3.8)	0.392
Stroke	1 (2.6)	1 (1.3)	0.550
Wound infection	3 (7.9)	4 (5.1)	0.682
Cardiac arrhythmia	3 (7.9)	5 (6.4)	0.716
Brain hemorrhage	2 (5.3)	1 (1.3)	0.250
Heart failure	5 (13.2)	4 (5.1)	0.151
Bleeding	3 (7.9)	1 (1.3)	0.102
Reoperation	3 (7.9)	1 (1.3)	0.102
CRRT	15 (39.5)	2 (2.6)	0.000
Hospitalization duration (d)	25.8 ± 28.4	15 ± 6.3	0.026
Ventilation use duration (d)	4.3 ± 14.4	1.6 ± 2.7	0.253
Any complications	25 (65.8)	20 (25.6)	0.000

Data are presented as number (%) or mean ± standard deviation.
CRRT, continuous renal replacement therapy.

Discussion

We compared the outcomes of open heart surgery in patients with ESRD on dialysis with those in a control

Table 6. Effects of dialysis on mortality and morbidity in multivariate analysis

Variables	Crude OR	*P* value	Adjusted OR	*P* value
Mortality				
In-hospital	8.6	0.010	14.7	0.033
After discharge	11.7	0.028	4.7	0.458
Total	11.6	0.000	10.7	0.029
Complications				
Pulmonary edema	9.0	0.002	10.7	0.067
Pneumonia	0.6	0.434	0.3	0.222
Sepsis	2.1	0.365	0	0.997
Wound infection	1.6	0.560	2.4	0.492
Cardiac arrhythmia	1.3	0.768	4.8	0.201
Brain hemorrhage	4.3	0.242	3.7	0.564
Heart failure	3.0	0.173	1.4	0.819
Bleeding	6.6	0.108	8.6	0.135
Reoperation	6.6	0.108	5.5	0.233
Postoperative CRRT	24.8	0.000	36.8	0.004
Hospitalization (> 20 d)	3.4	0.005	4.6	0.034
Mechanical ventilation (> 1 d)	3.7	0.021	7.6	0.022
Any complications	5.8	0.000	5.7	0.006

CRRT, continuous renal replacement therapy; OR, odds ratio.
Adjusted variables: age, sex, anemia, hypertension, hypercholesterolemia, and endocarditis.

Table 5. Relative risk of in-hospital mortality

Variable	Variable present		Variable absent		RR	Adjusted RR
	No. of death	Mortality (%)	No. of death	Mortality (%)		
Sex, male	8	9.1	1	3.6	2.5	1.7
Aged > 60 yr	4	13.8	5	5.7	2.4	1.1
Hypertension	8	11.0	1	2.3	4.7	2.0
NYHA IV	7	35.0	2	2.1	16.8	3.0
Endocarditis	3	23.1	6	5.8	4.0	1.7
ESRD on dialysis	7	18.4	2	2.6	7.2	6.9
Urgent surgery	8	15.7	1	1.5	10.2	2.1
Combined OP (valve/CABG)	3	14.3	6	6.3	2.3	0.8
High risk (EuroSCORE II)	3	23.1	6	5.8	4.0	1.6

CABG, coronary artery bypass grafting; ESRD, end-stage renal disease; NYHA, New York Heart Association; OP, operation; RR, relative risk.
Adjusted variables: age, sex, hypertension, diabetes mellitus, hypercholesterolemia, endocarditis, peripheral vascular disease.

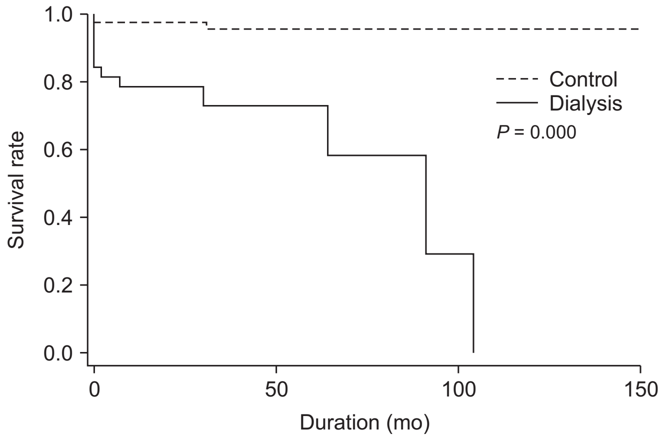

Figure 2. **Postoperative survival curve according to the Kaplan–Meier method.**

group with preserved renal function. More comorbidities, higher NYHA class at admission, and greater need for urgent surgery were identified in the dialysis group. The rate of urgent surgery in the dialysis group was extremely high, but the type of procedure and risk predicted by EuroSCORE II was not significantly different. In-hospital mortality was significantly higher in the dialysis group compared to the control group. We estimated the relative risk of mortality through several variables. After adjustment, the relative risk for mortality was the highest in ESRD on dialysis. No significant difference was observed between the dialysis and control groups in terms of EuroSCORE II. EuroSCORE II is used as a predictor of postoperative risk in the general population after open heart surgery, but it did not accurately predict postoperative mortality in the dialysis group [10,11]. EuroSCORE II has good predictive value, but the predictive power was limited in chronic dialysis patients. It may be associated with the fact that in chronic dialysis patients, multiple comorbidities mitigate the predictive power of EuroSCORE II.

The dialysis group exhibited a higher risk for mortality after open heart surgery. The causes of death could not be compared directly due to the low mortality rate. In previous studies, chronic dialysis patients showed increased postoperative risk for several reasons. First, chronic dialysis patients are immunocompromised owing to the presence of uremia or diabetes mellitus, steroid use for autoimmune causes of renal failure, and other unknown etiologies [12]. Second, they possess chronic anemic conditions due to the loss of erythropoietin production, and the presence of anemia is known to be associated with an increase of mortality after surgery [13–15]. Third, uremia may cause platelet dysfunction and coagulation defects, which may increase bleeding tendencies postoperatively [16]. Finally, arteriosclerosis, which is common in chronic dialysis patients, may increase the incidence of thromboembolic events and stroke [17]. In our study, the percentage of patients with diabetes mellitus was similar between the groups. However, the rate of hypertension, anemia, and endocarditis was significantly higher in the dialysis group.

There was no significant difference in postoperative complications except for pulmonary edema or frequency of CRRT use. However, the overall complication rate was significantly higher in the dialysis group. The higher frequency of CRRT therapy is expected during the immediate postoperative period because in chronic dialysis patients, maintenance dialysis is required during the hemodynamically unstable postoperative period.

The mortality rate after discharge was also significantly higher in chronic dialysis patients. We investigated the causes and duration until post-discharge death in both groups. One patient (1.28%) in the control group and five (13.16%) in the dialysis group died during the follow-up period until December 2017. The causes of death after discharge in the dialysis group were stroke, sepsis (n = 3), gastrointestinal bleeding (n = 1), and unknown (n = 1). In the control group, 1 patient died of stroke. The median duration until death after discharge in the dialysis group was longer than in the control group. The higher mortality rate after discharge in the dialysis group seemed to be associated with the higher mortality risk in the ESRD population compared to the normal control rather than the consequences of open heart surgery.

In summary, chronic dialysis patients exhibited higher postoperative mortality, longer hospitalization, and a higher overall rate of complications after open heart surgery compared to the control patients. Dialysis increased the overall mortality risk, especially during the in-hospital period. During the follow-up after discharge, dialysis patients also showed a higher mortality rate compared to the control patients with normal renal function.

In conclusion, chronic dialysis patients have a higher risk of postoperative mortality and morbidity after open heart surgery. Therefore, the benefits of surgical treatment must be balanced against the potential risks of open heart surgery in chronic dialysis patients.

Conflicts of interest

All authors have no conflicts of interest to declare.

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Authors' contributions

Sun-Hee Park and Gun Jik Kim participated in proposal of idea and designing the study. Jung Hwa Park, Jeong-Hoon Lim, Kyung Hee Lee, and Hanna Jung participated in data acquisition. Jung Hwa Park, Jang-Hee Cho, Sun-Hee Park, Hee-Yeon Jung, and Ji-Young Choi participated in data analysis and interpretation. Jung Hwa Park and Jeong-Hoon Lim participated in statistical analysis. Jung Hwa Park, Sun-Hee Park, and Ji-Young Choi participated in writing the paper. Sun-Hee Park, Jang-Hee Cho, Chan-Duck Kim, and Yong-Lim Kim participated in reviewing the paper and supervision or mentorship. Each author contributed important intellectual content during manuscript drafting or revision and accepts accountability for the overall work.

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