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ORIGINAL ARTICLE



Early Surgical Outcomes of Coronary Artery Bypass Grafting in Patients with Dialysis-Dependent Renal Failure: Effects of Early Hemodialysis

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Background: Coronary artery disease occurs frequently and is a major cause of morbidity and mortality in patients with chronic renal failure. Because the number of patients requiring dialysis for end-stage renal disease (ESRD) has increased, the number of patients in this population who require coronary artery bypass grafting (CABG) has increased. The aim of this study was to examine the effect of early hemodialysis (HD) on the early surgical outcomes of ESRD patients undergoing CABG. Materials and Methods: Fifty-nine dialysis-dependent patients who underwent isolated CABG with cardiopulmonary bypass (CPB) were enrolled in this study. These patients were divided into two groups based on the timing of the first postoperation HD session. In the early HD group, HD was performed within 6 h postoperation; in the scheduled HD group, HD was performed >6 h postoperation. The preoperative characteristics, operative variables, and postoperative outcomes were retrospectively analyzed. **Results:** The time to first HD after CABG was 2.43 ± 1.58 h in the early HD group and 20.68 ± 6.98 h in the scheduled HD group (P < 0.001). There were no significant differences in the operative variables, namely duration of operation, CPB time, and aortic cross-clamp time, between the two groups. The incidence of postoperative pneumonia was higher in the scheduled HD group (31.8%) than in the early HD group (2.7%). There was a trend of decreased incidence of postoperative pneumonia in the early HD group with marginal significance from the univariate analysis. The intensive care unit and hospital stay duration of both groups were similar. Nine patients died in the hospital, yielding an overall 30-day mortality of 8.47%. Conclusion: In dialysisdependent patients who underwent CABG, the short-term outcomes and surgical mortality were acceptable. Dialysis-dependent renal failure should not be considered a contraindication for CABG. Early HD in the postoperative period demonstrated the trend to reduce the incidence of postoperative pneumonia; however, other parameters of surgical outcomes were insignificant.

Key words: Coronary artery bypass grafting, end-stage renal disease, hemodialysis, surgical outcomes

INTRODUCTION

Patients with end-stage renal disease (ESRD) are at a high risk of cardiovascular disease, which accounts for almost half of all deaths of patients receiving hemodialysis (HD).¹⁻³ Due to the advancements in dialysis treatment, the prevalence of people living with ESRD has progressively increased. Patients with ESRD undergoing HD are at a high risk of increased morbidity and mortality following cardiac surgery.⁴⁻⁶

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Optimizing the perioperative management in dialysisdependent ESRD patients is crucial for short- and long-term outcomes.

In ESRD patients who have undergone coronary artery bypass grafting (CABG), impaired renal function results in several physiologic abnormalities that can contribute to adverse postoperative outcomes.^{7,8} HD was designed to accomplish three objectives: To remove solutes, alter the electrolyte concentration of the extracellular fluid, and remove various amounts of extracellular fluid. Managing the fluid and electrolyte balance is essential during the postoperative period, especially after cardiac surgery. Moreover, HD induces multiple beneficial changes in ESRD patients, several of which can favorably affect contractility. Contractility is likely to improve because dialysis involves the removal of uremic toxins and an increase in the ionized calcium and bicarbonate concentrations in the plasma. 9 Implementing renal replacement therapy early in critically ill patients with acute kidney injury may benefit patient survival. 10 A previous prospective study demonstrated that perioperative prophylactic HD reduces

both operative mortality and morbidity in patients with renal dysfunction.¹¹ However, the impact of early HD immediately after CABG and the early outcomes in patients with ESRD have not been studied.

The purpose of the current study was to evaluate and compare the short-term outcomes in patients with ESRD undergoing CABG by using either early HD (within 6 h postoperation) or scheduled HD (>6 h postoperation) policy.

MATERIALS AND METHODS

The institutional review board approved this retrospective observational study, and the approval included a waiver of informed consent (TSGH IRB No. 1-102-05-082).

Study patients

In this study, 59 patients (37 male and 22 female patients) with ESRD under maintenance HD who underwent a CABG procedure at our institution between January 2007 and December 2011 were retrospectively analyzed. Demographic and clinical data, including information on the patients' prior medical history, cardiac risk factors, operative details, and postoperative Intensive Care Unit (ICU) treatment course, were collected. Patients who underwent emergent or reoperative CABG or concomitant valve surgery, and those who experienced massive mediastinal bleeding requiring reoperation or received preoperative mechanical support, such as intraaortic balloon pumping and extracorporeal membranous oxygenation, were excluded from this study. The included patients were divided into two groups according to the time they underwent HD after the CABG operation in the ICU. The patients in the immediate HD group underwent HD within 6 h postoperation, whereas the patients in the scheduled HD group usually underwent HD on the day following the operation.

Surgical procedure

Coronary artery bypass grafting was performed through median sternotomy in both groups of patients and the operation was done with the utilization of cardiopulmonary bypass (CPB). CPB was established through standard aortocaval cannulation after heparinization (300 IU/kg) using a roller pump and hollow-fiber membrane oxygenator at moderate hypothermia (28°C-32°C) with pump flow rates of 2.0-2.5 L/min/m² to maintain a perfusion pressure of approximately 65 mmHg. When beating-pump technique was used, stabilization of the target arteries was accomplished with an Octopus II stabilizer (Metronic Inc., Minneapolis, MN, USA). With the application of suction from the stabilizer, the visualization and stabilization of the remote target arteries near the circumflex trunk was feasible. A humidified, sterile carbon dioxide "blower" was used to clear

the surgical field of blood. Meanwhile, medical reduction of heart rate and myocardial contractility was performed with a short-acting beta-blocker. In patients underwent cardioplegic arrest method, myocardial protection was carried out through anterograde and retrograde administration of cardioplegia with either blood or crystalloid solution. The anastomosis was carried out using a continuous 7-O prolene suture. After the anastomosis was completed, but before the suture was tied, a 2-mm probe was passed through the coronary artery to verify the patency of the anastomosis. After completion of the distal anastomoses, proximal anastomoses were sewn to the aorta under a partial occlusion clamp with 6-O prolene. During partial clamping and punching of the aorta, the site of plaque formation was avoided and the punching sites were carefully irrigated with diluted heparin solution. During CPB, the hematocrit was maintained between 20% and 25%. The goal was the complete revascularization of diseased coronary arteries with individual grafts, and the left internal thoracic artery was used as a conduit in all patients if possible. Radial arteries were not harvested, because of the existence of arteriovenous (AV) shunts, or reserved for creating AV shunts for HD in the future.

Perioperative renal management

All the patients referred for an elective CABG underwent dialysis on the day prior to their operation, and all of the patients underwent intraoperative hemofiltration during CPB. Postoperatively, dialysis commenced after hemodynamic stabilization in all patients in the ICU. The patients underwent HD within 6 h were mostly hemodynamic stable, but showed symptoms and signs, including fluid overloading, relatively poor oxygenation or electrolyte problem that may be corrected after immediate HD. Some patients with unstable hemodynamic condition, large amount of mediastinal drainage were not suitable for immediate HD. HD was performed using a volume-controlled dialysis machine (AK 200 S; Gambro, Lund, Sweden) and a polyamine S membrane hollow-fiber dialyzer (Polyflux L; Gambro, Lund, Sweden). The dialysate fluid contained 139 mEg/L of sodium, 2.0 mEg/L of potassium, 1.0 mEq/L of magnesium, 3.5 mEq/L of calcium, 106.5 mEq/L of chloride, 4.0 mEq/L of acetate, 35 mEq/L of bicarbonate, and 200 mg/dL of dextrose. The dialysate temperature was set at 36°C. The dialysate flow rates were set at 500 mL/min, whereas the blood flow rates were 250-350 mL/min. The duration of each HD session was 4-5 h.

Statistical analysis

All statistical analyses were performed using the statistical software SPSS for Windows version 17.0 (SPSS, Chicago, IL, USA). The descriptive statistics were expressed as the mean \pm standard deviation. The Student's *t*-test was used to

investigate the continuous variables and the Chi-square test was used to compare the categorical variables between groups. Multivariate logistic regression analysis was performed to evaluate the odds ratio of potential predictors of post-CABG pneumonia in ESRD patients. Statistical significance was assumed if the P < 0.05.

RESULTS

Patient profiles

The time to HD was 2.43 ± 1.58 h in the early HD group and 20.68 ± 6.98 h in the scheduled HD group (P < 0.001). The preoperative patient profiles are summarized in Table 1. The patient demographics and preoperative variables, except age, did not exhibit significant differences between the early and scheduled HD groups. The duration of HD in the early HD group and scheduled HD group were 54.81 ± 87.75 months and 44.81 ± 44.43 months, respectively (P = 0.622). The mean preoperative creatinine levels of both groups were similar and higher than 6.0 mg/dL. The prevalence of comorbidities, such as chronic obstructive pulmonary disease and previous cerebral vascular accident, and coronary risk factors, such as hypertension, diabetes mellitus, and hyperlipidemia, was similar in both groups of patients. The percentage of patients with a previous myocardial infarction, New York Heart Association functional class, and left ventricular (LV) ejection fraction $(53.27 \pm 14.21\%)$ in the early HD group vs. $51.27 \pm 12.94\%$ in the scheduled HD group) indicated no statistical significance.

Operative data

Coronary artery bypass grafting was performed with a mean of approximately 3 distal anastomoses and the left internal mammary artery was used in 74.6% of patients. There were no significant differences in operative variables such as duration of operation, CPB time, and aortic cross-clamp time between the groups [Table 2].

Early outcomes

Table 3 shows a comparison of the clinical outcomes between the 2 groups. The mechanical ventilation times and inotropic scores of both groups were similar. There was a significantly higher incidence of postoperative pneumonia in the scheduled HD group (31.8%) compared with the early HD group (2.7%; P = 0.006). The ICU and hospital stay duration of both groups were similar, and five patients died in the hospital, yielding an overall 30-day mortality of 8.47%. The in-hospital mortality rates for patients in the early HD group and scheduled HD group were 5.4% (n = 2) and 13.6% (n = 3), respectively (n = 2) and 13.6% (n = 3), respectively (n = 2).

Overall, eight patients developed postoperative pneumonia, yielding a prevalence of 13.6%. The risk factors for the development

of postoperative pneumonia determined by performing univariate analysis are shown in Table 4. In the univariate analysis, old age, long ICU stay, and high central venous pressure level were associated with postoperative pneumonia. The results of the multivariate logistic regression analysis are shown in Table 5. A significant risk factor for postoperative pneumonia was belonging to the scheduled HD group (odds ratio 27.01; P = 0.025).

DISCUSSION

This retrospective analysis yielded several findings. First, in dialysis-dependent patients who undergo CABG, the short-term outcomes and surgical mortality are acceptable. Although the perioperative risk of dialysis-dependent patients is higher

Table 1. Preoperative status of patients with end-stage renal disease undergoing CABG

Characteristic	Early HD $(n = 37)$	Scheduled HD $(n = 22)$	P value
Ages (years)	63.42±12.48	68.00±11.52	0.016
Sex (male/female)	23/14	14/8	0.910
Creatine (mg/dL)	6.56±2.76	6.89±3.22	0.675
Preoperative hemoglobin (mg/dL)	9.46±1.40	9.82±1.50	0.359
Duration of dialysis (month)	54.81±87.75	44.81±44.43	0.622
Hypertension (yes/no)	20/17	12/10	0.971
Diabetes (yes/no)	24/13	15/7	0.795
COPD (yes/no)	20/17	15/7	0.412
PVD (yes/no)	3/34	3/19	0.661
CVA (yes/no)	3/34	3/19	0.661
NYHA classification >III (no)	10	5	0.767
Previous MI (no)	4	3	0.746
EF (%)	53.27±14.21	51.27±12.94	0.592

CABG = coronary artery bypass grafting; SLE = systemic lupus erythematous; COPD = chronic obstructive pulmonary disease; PVD: peripheral vascular disease; NYHA = New York Heart Association; CCS = canadian Cardiovascular Society; MI = Myocardial infarction; HD: hemodialysis; CVA = cerebral vascular accident; EF = ejection fraction

Table 2. Operative data

Operative variable	Early HD $(n = 37)$	Scheduled HD $(n = 22)$	P value
Beating pump CABG (yes/no)	12/25	5/17	0.556
Number of distal anastomoses (no)	2.95±0.66	2.95±0.65	0.962
LIMA use (no)	27	7	0.767
Duration of operation (min)	317.84±50.04	321.14±44.02	0.793
CPB time (min)	126.27±66.98	123.18±39.16	0.845
Aortic cross-clamp time (min) ^a	59.49±40.33	58.23±23.36	0.894

^aExcluded off-pump CABG patients; CABG = coronary artery bypass grafting; LIMA = left internal mammary artery; CPB = cardiopulmonary bypass; HD = hemodialysis

Table 3. Postoperative recovery course

Variable	Early HD $(n = 37)$	Scheduled HD $(n = 22)$	P value
Mechanical ventilation (h)	53.70±39.94	79.06±77.39	0.222
Ventilator dependence (yes/no) ^a	7/28	4/15	0.748
Time to HD (h)	2.43±1.58	20.68±6.98	< 0.001
Inotropic score	20.87±23.12	17.81±15.61	0.585
PCWP (mmHg)	20.11±7.29	19.23±4.44	0.566
LCOS (yes/no)	2/35	0/22	0.524
Arrhythmia (yes/no)	4/33	0/22	0.286
Stroke (yes/no)	2/35	1/21	0.884
Pneumonia (yes/no)	1/36	7/15	0.006
Wound infection (yes/no)	4/33	0/22	0.286
ICU stay (days)	8.80±11.96	11.64±9.57	0.348
Hospital stay (days)	33.86±28.07	32.55±25.62	0.858
Surgical mortality (yes/no)	2/35	3/19	0.272

^aExcluded surgical mortality patients; PCWP = pulmonary capillary wedge pressure; LCOS = low cardiac output syndrome; ICU = intensive care Unit; HD = hemodialysis

Table 4. Characteristics of patients with or without pneumonia after CABG

Variable	No postoperative pneumonia ($n = 51$)	Postoperative pneumonia $(n = 8)$	P value
Age (year)	63.82±12.11	73.50±9.94	0.036
TTHD (h)	8.53±10.29	13.75±5.70	0.052
LVEF (%)	52.53±14.24	52.50±10.02	0.996
Pump time (min)	125.69±61.24	121.50±29.78	0.851
Clamping time (min)	60.27±36.62	51.00±18.45	0.488
CPB I/O (negative)	209.41±216.40	650.00±879.12	0.200
Potassium (mg/dl))	4.50±0.78	4.13±0.33	0.028
Post pH	7.37±0.07	7.41±0.08	0.209
Hospital stay (day)	31.59±24.66	44.75±38.92	0.202
Intropic score	18.17±20.23	29.66±21.07	0.143
ICU stay (day)	8.44±10.64	18.88±10.51	0.012
PCWP (mmHg)	19.45±5.75	21.86±9.58	0.319
I/O (kg)	1.62±1.31	0.80±1.00	0.096
CVP	14.43±4.34	19.86±5.69	0.003

TTHD = time to hemodialysis; LVEF = left ventricular ejection fraction; CPB = cardiopulmonary bypass; ICU = intensive care unit; PCWP = pulmonary capillary wedge pressure; CVP = central venous pressure; CABG = coronary artery bypass grafting

than normal, it is not prohibitive, and ESRD should not be considered a contraindication for CABG. Second, early HD in the postoperative period demonstrated the trend to reduce the incidence of postoperative pneumonia with marginal significance; however, other parameters of surgical outcomes were insignificant.

Table 5. Multivariate logistic regression analysis for patients with postoperative pneumonia

Factor	OR (95% CI)	P value
Sex	0.370 (0.043-3.162)	0.364
Age (>65)	0.690 (0.082-5.811)	0.733
Scheduled HD group	27.01 (1.502-485.70)	0.025
Smoking	1.164 (0.110-12.35)	0.899
Inotrope score	1.049 (0.997-1.104)	0.064

OR = odds ratio; CI = confidence interval; HD = hemodialysis

The treatment options for coronary artery disease include percutaneous transluminal coronary angioplasty (PTCA) and CABG. However, the restenosis rate after PTCA is high, and aggressive restenosis limits the long-term clinical benefits of this treatment.12 CABG may be a reasonable treatment option for dialysis-dependent patients with coronary artery disease refractory to medical therapy because of improved overall and symptom-free survival compared with PTCA.¹³ The long-term survival of HD patients who underwent CABG was observed to be equivalent to that of HD patients who did not undergo myocardial revascularization.¹⁴ Thus, despite the high early mortality, CABG effectively enables HD patients to recover their life expectancy curve. However, concerns of high perioperative mortality rates following CABG have maintained doubts regarding the benefits of CABG among patients with ESRD. In recent times, several series of cardiac operations performed on dialysis-dependent patients have been published.¹⁵ The in-hospital mortality rate of these patients was reported to be as high as 36.7%, and was dependent on the complexity of cardiac operations. The surgical mortality rate after isolated CABG in dialysis-dependent patients was reported to be approximately 10%, which was higher than that for PCI. 16,17 With an in-hospital mortality rate of 8.47%, our results are comparable with these findings. In a large study, the operative mortality rates and lengths of in-hospital stay have substantially declined in ESRD patients undergoing CABG.¹⁸ Nonetheless, patients with dialysis-dependent renal failure before operation exhibit a substantially higher risk for early and late mortality and higher complication rates than nondialysis patients do. 19-21 These observations indicate that improving perioperative management procedures is necessary.

The higher mortality and morbidity of CABG in ESRD patients may be attributed to several reasons. First, most patients with renal insufficiency demonstrate LV hypertrophy and subsequent subendocardial ischemia secondary to arterial hypertension even prior to ESRD requiring dialysis.²² Second, a uremic environment is cardiotoxic and can result in LV dysfunction. This is supported by a prospective 10-year study on patients with ESRD in which renal transplantation dramatically improved LV abnormalities.²³ Another crucial

factor is hyperparathyroidism secondary to renal failure, which was shown to be associated with atherosclerosis and the calcification of cardiac structures, including the valves and condition tissue.²⁴ Third, factors associated with ESRD can mask clinical symptoms.²⁵ It was reported that, even in the presence of substantial coronary artery disease, patients with ESRD experience little or no angina pain, which is probably the result of diabetic or uremic polyneuropathy, or both.²⁶ Moreover, even a coronary stenosis of >90% would have been overlooked in 30% of these patients.²⁵ All of these data suggest that both indications and referrals for CABG can be delayed in patients with ESRD who also have significant coronary artery disease.

The optimal management of fluid balance and electrolyte concentrations is crucial for ESRD patients during the postoperative period. Cardiac and renal functions are interrelated, with each system having considerable influence on the other. An invasive study conducted on both dialysis and predialysis patients revealed that cardiac performance may be impaired early in the development of renal failure.²⁷ Although HD may benefit ESRD patients and improve LV performance,9 the performance of dialysis in the early postoperative period may be complicated by abrupt changes in cardiopulmonary and hemodynamic functions (despite the current improvements in dialysis techniques). The sophisticated management of fluid, electrolyte balance, and hemodynamic monitoring are mandatory for postoperative outcomes. Although the other surgical outcomes were similar, there was a significantly higher incidence of postoperative pneumonia in the scheduled HD group (31.8%) compared with the early HD group (2.7%; P = 0.006) in this study. These results are consistent with those previously reported by Iyem et al., 28 who concluded that early dialysis for open-heart surgery patients who postoperatively develop acute renal failure reduces major complications such as postoperative pneumonia.

Because chronic dialysis is a crucial risk factor for morbidity and mortality, efforts have been made to improve the outcomes of CABG in ESRD patients. Particularly in the case of dialysisdependent patients who have undergone heart surgery, problems associated with CPB-like fluid and electrolyte hemostasis, hemodilution, and coagulation disorders require optimal management to limit perioperative risk and improve surgical outcomes. Both knowledge and careful consideration of these factors specific to chronic kidney disease can help optimize perioperative management in the nonhomogeneous group of ESRD patients who have undergone CABG. Knowledge of these factors has become even more critical because of the increasing number of patients requiring dialysis and hence, subsequent CABG.²⁹ The close collaboration of nephrologists, cardiologists, and cardiac surgeons is necessary for improving the clinical outcomes in this population of patients.

This study has several limitations. First, this was a nonrandomized and retrospective study from a single institution; therefore, the findings are susceptible to various sources of bias. Second, although comparable to that of previous studies, the number of study patients was limited. Third, the site of an AV fistula for HD was not included as a variable, but we used internal thoracic arterial grafts for revascularization in most patients who underwent CABG. Definitively no reports have documented coronary artery steal with an ipsilateral AV fistula. However, there have been several reports of coronary steal, particularly in patients with an extremely high-flow AV fistula. 30,31

CONCLUSION

Coronary artery bypass grafting can be safely and effectively performed in dialysis-dependent ESRD patients. When applicable, early HD in post-CABG patients demonstrated the trend to reduce the incidence of pneumonia from the present study, but other parameters of surgical outcomes were insignificant. More randomized and prospective studies are necessary to clarify the effects of early HD in the outcomes after CABG. Due to the increasing prevalence of patients undergoing HD, especially in Taiwanese society, our findings may provide crucial information for clinical care.

DISCLOSURE

The authors declare no conflicts of interest in conducting this study.

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