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Review Article

Coronary Artery Bypass Surgery in End-Stage Renal Disease Patients

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The number of patients requiring hemodialysis is continuously increasing around the world. Hemodialysis affects patient quality of life and it is also associated with a higher risk for cardiovascular events. In addition to traditional risk factors for cardiovascular events such as hypertension, hyperlipidemia, and diabetes, hemodialysis is associated with hyperphosphatemia, chronic inflammation, vascular calcification, and anemia which accelerate atherosclerosis, vascular stiffness, and cardiac ischemia. Treatment strategy for coronary revascularization in this progressive disease remains controversial. However, a systematic treatment including medical therapy and complete revascularization through a less invasive strategy should be considered in addressing this problem. This review discusses the epidemiology, vascular pathology and current treatment options in patients with end-stage renal disease requiring coronary revascularization.

Keywords: end-stage renal disease, CABG, PCI, hemodialysis

Introduction

Development of hemodialysis has brought a new era of medical therapy for patients with end-stage renal disease. Although this technology may prolong life for patients with failing kidneys, the long-term outcomes of these patients remain poor. The overall 5-year survival of patients undergoing hemodialysis is only 55–60%. Cardiovascular complications are often reported in these patients and is the leading cause of death in this population.[1–4]

In 2010, 2.6 million patients received hemodialysis treatment worldwide. However, it is estimated that at least 2.2 million patients did not have access to this treatment. The majority of these patients reside in developing countries, particularly in Asia and Africa with an estimated number of 1.9 million and 432,000 patients, respectively. It is also estimated that, due to the continuously increasing incidence of diabetes, the number of patients requiring hemodialysis will double to approximately 5.4 million patients by 2030.[5]

This review discusses the epidemiology, vascular pathology, treatment, and long-term outcomes for patients with end-stage renal disease requiring coronary artery revascularization.

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Current Status of Dialysis

Number of patients and current hemodialysis

The number of patients with end-stage renal disease in the United States exceeded 320,000 in 1998 and has increased to 660,000 in year 2015.[6] The prevalence across all age groups varies from 6% to 16% and is the highest in Japan and Taiwan.[1] Patients requiring hemodialysis are continuously increasing in Japan, with more than 320,000 cases reported in 2014. However, according to the Dialysis Outcomes and Practice Patterns Study (DOPPS), 1-year mortality rate in Japan was the lowest (6.6%) compared to Europe (15.6%) and the United States (21.7%).[7,8] The most recent data from the Japanese Society for Dialysis Therapy showed 1-year, 5-year, and 10-year survival rates of 89.9%, 60.8%, and 35.9%, respectively. In conventional hemodialysis, patients are required to have hemodialysis treatment 3 days a week, which provides an estimated creatinine clearance of 10 ml/min. Recently, home hemodialysis is becoming widespread around the world, providing creatinine clearance of 40 ml/min through daily home nocturnal hemodialysis. Although this system is rarely used, it may provide more efficient renal therapy in patients with end-stage renal disease.[9]

Cause of the disease

Many patients with end-stage renal disease have underlying diseases such as diabetes and hypertension. Approximately, 40% of end-stage renal disease cases are caused by diabetic nephropathy and hypertension is prevalent in 60–100% of patients with chronic kidney disease.[10] Hyperlipidemia is also highly associated with chronic kidney disease, with elevated total cholesterol observed in 30%

of all chronic kidney disease patients and up to 90% of patients with nephrotic syndrome.[10]

Diabetes is associated with many comorbidities other than end-stage renal disease, including peripheral artery disease, acute myocardial infarction, and stroke. However, due to recent advances in medical therapy, the incidence of such comorbidities is decreasing. From 1990 to 2016, the largest decrease in comorbidity incidence was observed for acute myocardial infarction (−67.8%; 95% confidence interval [CI] −76.2 to −59.3). Despite this decreasing incidence, end-stage renal disease showed the least decline (−28.3%; 95% CI −34.6 to−21.6).[11]

Cause of death

Almost half of the deaths in patients with end-stage renal disease are caused by cardiac diseases including heart failure and myocardial infarction. Coronary artery disease is common in this set of patients and is strongly associated with adverse events.[12] A report by the National Kidney Foundation has shown a high prevalence of cardiovascular disease in patients with chronic kidney disease, and a 10–30-fold higher mortality rate in patients with end-stage renal disease compared to the general population.[6,13–17] Parfrey et al. showed that the 2-year cumulative survival rate for patients with end-stage renal disease and congestive heart failure was as low as 33%.[18]

Traditional cardiovascular disease risk factors such as diabetes, hypertension, advanced age, left ventricle hypertrophy, and hyperlipidemia, are often prevalent in patients with end-stage renal disease. In addition to these known risk factors, patients with end-stage renal disease are characterized by non-traditional suggested factors including anemia, fluid volume overload, inflammation, electrolyte imbalance, malnutrition, altered nitric oxide/endothelin balance, abnormal calcium/phosphate metabolism, and oxidative stress.[6,19,20] The AURORA trial has shown that baseline albumin (hazard ratio [HR] 0.96; 95% CI 0.94–0.99 per g/l increase), high-sensitivity C-reactive protein (CRP) (HR 1.13; 95% CI 1.04–1.22 per mg/l increase) and oxidized low-density lipoprotein (LDL) cholesterol (HR 1.09; 95% CI 1.03–1.17 per 10 U/l increase) were significant predictors of atherosclerotic event development.[21]

In a series of incidental consecutive cardiac catheterization in patients with hemodialysis, significant coronary artery stenosis, defined as more than 75% narrowing of a major coronary artery, was observed in more than 60% of patients, with an average of 3.3 lesions per patient.[22] At least 35% of patients with chronic kidney disease have myocardial ischemia or angina at the time of referral to the nephrologist.[23] Hospital mortality rate due to acute myocardial infarction is higher for patients with chronic kidney disease (normal renal function 2%, mild disease 6%, moderate disease 14%, severe disease 21%, and hemodialysis 30%).[24] Moreover, 1-year mortality after acute myocardial infarction is reported between 59–66% in patients with moderate disease or hemodialysis.[10,25]

Vascular Lesions in End-Stage Renal Disease

Elevated levels of CRP, interleukin-6 (IL-6), and fibrinogen are also observed in patients with chronic kidney disease which is also linked with increased cardiovascular risk.[26,27] In patients with chronic kidney disease, elevated CRP was significantly associated with major cardiac adverse events (1 mg/l increment in CRP was associated with HR 1.94; 95% CI 1.27–2.94). CRP has also been suggested to be useful in predicting patients with progression of coronary atherosclerosis (positive prediction of coronary events 65%; negative prediction 74%).[27]

Interaction between systemic inflammation, malnutrition, and atherosclerosis leads to the malnutrition-inflammation-atherosclerosis/calcification (MIAC) syndrome, with pro-inflammatory cytokines playing a major role in this progressive pathology.[26] Thoracic peri-aortic fat tissue increases in patients with end-stage renal disease and is positively correlated with CRP, MIAC syndrome, and calcified valves.[28] It has also been shown to have a positive correlation with age, Body Mass Index (BMI), uric acid, thoracic aortic calcification and coronary artery calcification.[29] Epicardiac adipose tissue is also known to be associated with pro-atherogenic cytokines, including tumor necrosis factor (TNF)-alpha, monocyte chemotactic protein (MCP-1), IL-6, and resistin. This adipose tissue covers 80% of the cardiac surface and is also known to be associated with MIAC syndrome.[26] Poppelaars et al.[30] showed the important role of mannose-binding lectin (MBL), an acute-phase protein increased during inflammation, in predicting cardiovascular risk in hemodialysis patients. The mannose-binding protein is the main initiator of the lectin pathway, one of the three activation pathways of the complement system. Although there was no significant difference in the levels of MBL between patients on hemodialysis compared to the general population, low MBL has been associated with cardiovascular events. It has been suggested that low MBL increases cardiovascular risk by promoting atherosclerosis due to the defective removal of atherogenic particles. Low MBL has also been associated with an increase in arterial stiffness.[30,31]

Vascular calcification and atherosclerosis causes a decrease in arterial elasticity, leading to increased arterial stiffness and pulse wave velocity. As the stiffness increases, the speed of forward wave to the periphery increases resulting in earlier arrival of the backward wave to the ascending aorta. This causes an increase in systolic pressure

and decrease in diastolic pressure.[32] This decrease in diastolic pressure leads to a reduction in coronary perfusion, and the increase in systolic pressure results in additional afterload to the left ventricular workload, leading to left ventricular hypertrophy.[33–35] Furthermore, decrease in the stiffness gradient between proximal elastic arteries and distal muscular arteries results in increased forward pressure to the peripheral microcirculation, causing end-organ damage.[32]

Calcification of the vascular system

A novel blood test (T50), measures calcification propensity of the blood by evaluating the transformation time from primary to secondary calciprotein particles.[36] In the EVOLVE trial, T50 was independently associated with all-cause mortality, myocardial infarction and hospitalization for unstable angina, heart failure, or peripheral vascular event.[37]

Vascular calcification in end-stage renal disease is described by the calcification of the intima and the media. Calcification of the intima is observed in the coronary artery, carotid artery, and the aorta, and is associated with atherosclerosis due to hyperlipidemia, hypercholesterolemia, and diabetes. Calcification of the media, also known as Monckeberg's sclerosis, is specific to patients with chronic kidney disease. This is mainly caused by hyperphosphatemia and observed in muscular arteries including the tibial and femoral arteries.[26,38] Fibroblast growth factor has also been reported to be associated, via alteration of minerals and parathyroid hormones, with both aortic and peripheral vascular calcification in patients with chronic kidney disease.[39]

Hyperphosphatemia

Hyperphosphatemia is observed in patients with chronic kidney disease due to impaired renal secretion of phosphate.[40] It is associated with a 41% increase in cardiovascular deaths and a 20% increase in risk of sudden death. Along with systemic inflammation, systemic calcification is advanced in end-stage renal disease patients. Jono et al. reported that in ex vivo human cultured vascular smooth muscle cells, high concentration of phosphate in the medium resulted in calcification of the cells.[41] Evidence from another ex vivo study using rats, showed that hyperphosphatemia resulted in calcification of the vascular media as observed via X-ray spectroscopy and electron microscopy.[42]

Treatment of hyperphosphatemia includes dietary restriction and use of phosphate binders. However, strict restriction of phosphate intake may lead to low protein intake and eventually to malnutrition, which is a strong risk factor for mortality in patients with end-stage renal disease.[40,43] Phosphate binders have been used to excrete phosphate from the system. However, aluminum-based phosphate binders are now prohibited due to their toxicity, which is associated with encephalopathy and bone disease. Use of calcium-based phosphate binders is also limited due to the risk of hypercalcemia, parathyroid gland suppression, and systemic calcification.[40] Non-calcium based binders including sevelamer, lanthanum carbonate and magnesium salt are now available for these patients.[40] Magnesium has been reported to inhibit vascular calcification induced by hyperphosphatemia and is associated with a decreased risk of cardiovascular mortality in hemodialysis patients.[44] Parathyroidectomy should also be considered in patients with long hemodialysis treatment and secondary hyperparathyroidism.[38]

Ischemic Heart Disease in Dialysis Patients

In addition to coronary artery stenosis through vascular calcification and atherosclerosis, patients with end-stage renal disease may have secondary ischemia due to a mismatch in oxygen demand and supply. An increase in aortic compliance through atherosclerosis leads to increased pulse wave velocity consequently resulting in systolic hypertension and eventually left ventricular hypertrophy.[45,46] Furthermore, arteriovenous blood access leads to systemic volume overload and eventually to an increase in left ventricular mass, diameter, and oxygen demand. Cox regression analysis, including age, diabetes, smoking, and homocysteine showed that 1 g/m(2.7)/month increase in left ventricular mass index was associated with a 62% increase in cardiovascular events (HR 1.62; 95% CI 1.13–2.33).[47] As chronic kidney disease progresses, the prevalence of left ventricular hypertrophy also increases, reaching 75% at the time of hemodialysis.[23] Decreased secretion of erythropoietin leads to chronic anemia and eventually to a decrease in oxygen supply. Walker et al. suggested that anemia is a risk factor for cardiovascular disease in patients with elevated serum creatinine.[48] In that study, the risk for hospitalization with myocardial infarction was 2–5-fold higher in patients with anemia (Hb$<$12g/dl).[48] In patients with end-stage renal disease, decreased cardiac function, and symptoms of heart failure often precede coronary artery stenosis. In addition, early symptoms of cardiac ischemia may be under diagnosed due to the high prevalence of diabetes in this population. Despite the presence of anemia, which may facilitate the detection of myocardial ischemia by putting patients into hypotension and hypovolemia during hemodialysis, 40% of the patients had silent ischemia as demonstrated by Holter monitoring.[49] The examination of the coronary artery in the outpatient clinic is also limited as use of contrast agents is restricted in patients with chronic kidney disease and end-stage renal disease.[50]

Coronary Artery Revascularization Method

PCI vs. CABG

The Arterial Revascularization Therapies Study (ARTS) showed that in patients with chronic kidney disease, there was no significant difference in operative death, myocardial infarction, and stroke for those treated by either coronary artery bypass grafting (CABG) or percutaneous coronary intervention (PCI) (adjusted HR CABG vs. PCI = 0.93; 95% CI 0.51–1.60, p = 0.97). However, CABG was associated with a lower risk for repeat revascularization (HR = 0.28; 95% CI 0.14–0.54).[51] Reddan et al. showed that for each 10 ml/min decrease in creatinine clearance there was an increase in mortality (HR 1.14, p < 0.0001). For patients with severe chronic kidney disease (creatinine clearance 15–29 ml/min), CABG was associated with a decreased mortality rate compared to PCI.[12] Charytan et al. reported higher mortality rates for the first 3 months in patients who underwent CABG compared to PCI (1.25; 95% CI 1.12–1.40). However, this trend was reversed after 6 months, with CABG patients showing lower mortality rates than those who underwent PCI (0.61; 95% CI 0.55–0.69).[52]

There are no randomized controlled trials comparing CABG with PCI in patients undergoing hemodialysis, and the optimal revascularization method for these patients remains controversial.[53] Baek et al.[54] reported a mean follow-up period of 50 months in hemodialysis patients in need of coronary revascularization. Of the 87 hemodialysis patients included in the study, 44 patients underwent drug-eluting stent (DES) implantation and 43 underwent CABG surgery. The major adverse cardiac and cerebral event (MACCE)-free survival was significantly higher in the CABG group compared to the DES group after propensity score matching (HR 3.265; 95% CI 1.357–7.858). However, there was no significant difference in overall survival between the two groups (HR 0.968; 95% CI 0.267–3.507).[54] A study conducted by the United States Renal Data System analyzed data from 21,981 hemodialysis patients requiring coronary revascularization. CABG was associated with a lower 5-year mortality rate (HR 0.87; 95% CI 0.84–0.90), and the composite of death or myocardial infarction (HR 0.88; 95% CI 0.86–0.91) compared to PCI.[55]

CABG early outcomes

Patients undergoing hemodialysis are at higher risk for operative mortality compared to non-hemodialysis patients. A total of 1,300 hemodialysis-dependent patients were compared to 18,387 non-hemodialysis patients who underwent isolated CABG from the Japan Adult Cardiovascular Surgery Database.[56] The 30-day mortality rate (4.8% vs. 1.4%), operative mortality (7.8 vs. 2.1%), and operative mortality and major complication (23.1% vs. 13.7%) were significantly higher in hemodialysis patients compared to non-hemodialysis patients, respectively.[56] In a prospective study including 15,500 patients undergoing CABG in the United States, hemodialysis patients had 3.1-fold (95% CI 2.1–4.7) higher mortality rates compared to those not undergoing hemodialysis. Patients on hemodialysis compared with non-dialysis patients were also more likely to develop postoperative mediastinitis (3.6% vs. 1.2%, respectively, adjusted odds ratio [OR] 2.4; 95% CI 1.2–4.7) and stroke (4.3% vs. 1.7%, respectively, adjusted OR 2.1; 95% CI 1.1–3.9).[57] On the other hand, studies have reported similar operative results between patients with or without hemodialysis. In a series of 23 hemodialysis patients and 69 matched non-dialysis patients, Kan et al. reported no significant differences in intubation time, intensive care unit stay, major complications, and 30-day mortality. Only patients with uremia were at greater risk for bleeding, longer postoperative stays, and late mortality.[1] Powell et al. showed that patients undergoing hemodialysis had longer hospital stays than patients without dialysis, but did not report significant differences in perioperative morbidity and mortality.[58] These reports however, are underpowered due to their small sample size.

Perioperative factors associated with early death in hemodialysis patients undergoing CABG include advanced age, chronic obstructive pulmonary disease, peripheral artery disease, poor left ventricle function, female gender, need for preoperative intra-aortic balloon pump, use of cardiopulmonary bypass, concomitant surgery, Canadian Cardiovascular Society (CCS)/New York Heart Association (NYHA) functional class IV, incomplete revascularization, and postoperative need for continuous hemofiltration.[59–61] Postoperative factors associated with early outcomes include stroke, infection, prolonged ventilation, pneumonia, heart block and gastrointestinal complications.[56]

CABG long-term outcomes

The ASCERT study showed that the estimated mortality rate in the general population who underwent CABG was 3.2%, 6.4%, 8.1%, and 23.3% at 30 days, 180 days, 1 year, and 3 years, respectively.[59] Patients with chronic kidney disease had higher mortality rate during the follow-up period compared to the general population. However, the mortality rate remained low for those who survived to hospital discharge. The mortality rate in patients with stage 3 and stage 4–5 chronic kidney disease was 0.006 and 0.009 deaths per year, respectively.[52]

For patients with end-stage renal disease, Ariyoshi et al. reported overall 5-year survival rates of 63.7%, cardiac-related 5-year survival rate of 89.3%, and a cardiac event-free rate of 51.7% following CABG.[62] Sezai

et al. reported that postoperative survival rate in 90 hemodialysis patients who underwent CABG was 81.5%, 72.0%, and 68.4% at 1, 5, and 8 years, respectively. The postoperative MACCE-free rate was 70.3%, 61.8%, and 58.6%, respectively.[60] In another study by Takami et al. (152 patients), the survival rates were 76.9%, 60.0%, 43.9%, and 36.2% at 3, 5, 8, and 10 years, respectively. The cardiac event-free rates were 77.0%, 70.1%, 55.9%, and 44.8%, respectively.[63]

The survival rates in end-stage renal disease patients who underwent CABG were comparable to those observed in end-stage renal disease patients who did not undergo CABG at 1 year (CABG 90.9% vs. no CABG 91.9%); 2 years (95.5% vs. 77.7%); 3 years (71.4% vs. 70.3%); and 5 years (40.0% vs. 40.3%, respectively).[64] CABG, together with intensive perioperative care, can offer favorable outcomes in end-stage renal disease patients. Moreover, it has been reported that CABG provides improved long-term outcomes compared to optimal medial therapy for patients undergoing hemodialysis.[26]

Predictors for late cardiac events include advanced age (>63 years), diabetes, and peripheral artery disease, whereas, predictors for late death include diabetes and left ventricular ejection fraction less than 0.40.[59] Higher ejection fractions have been associated with improved survival rates during the follow-up period. In contrast, a history of stroke, transient ischemic attack, reversible ischemic neurological deficit, chronic lung disease, and immunosuppressive treatment have been linked to poor survival rates during the follow-up period.[59] In addition, it has been noted that the magnitude of effect of important predictors, such as current smoking, insulin-dependent diabetes, and hemodialysis on survival increased over time. This suggests an accumulation of risk in patients undergoing hemodialysis.[53]

Graft selection

In the general population, a meta-analysis showed that use of three arterial grafts was independently associated with a reduction in long-term mortality rates (HR 0.8; 95% CI 0.75–0.87; $p<0.001$).[65] Use of the right gastroepiploic artery was also reported to be a significant predictor for cardiac event-free survival.[66] The early patency rates of arterial grafts prior to hospital discharge were satisfying (between 97–100%) in the left anterior descending, diagonal, obtuse marginal, posterolateral, posterior descending, and right coronary arteries.[67]

Use of the radial artery for patients undergoing hemodialysis is limited as this vessel is involved in arteriovenous blood access. During arteriovenous blood access, the steal phenomenon may also occur due to an inner shunt in the internal thoracic artery. Saphenous vein grafts may also be used, considering the possibility of subsequent distal bypass, as patients undergoing hemodialysis are at higher risk for developing peripheral artery disease. Patients with chronic kidney disease have more than 2-fold increased risk of developing peripheral artery disease.[68–72] According to a report by the United States Renal Data System (USRDS), the incidence of clinical peripheral artery disease in hemodialysis patients is 15%.[73]

In a study by Kinoshita et al. among 56 hemodialysis patients who underwent coronary artery bypass, bilateral internal thoracic arteries (BITA) and single internal thoracic arteries (SITA) were used in 32 and 23 patients, respectively. After adjusting for propensity score, patients with BITA were not at higher risk for mediastinitis (OR 0.63; 95% CI 0.04–8.79). Also, the 30-day mortality rates (OR 0.60; 95% CI 0.05–6.82) were also similar between the two groups.[74] Progression of systemic calcification in patients with end-stage renal disease limits the use of aortic clamping due to the risk for cerebral embolization, restricting the use of free graft on the aorta.[75]

Off-pump CABG vs. on-pump CABG

A meta-analysis of 100 randomized controlled trials including a total of 19,192 subjects did not identify significant differences in the early all-cause mortality rates (OR 0.88; 95% CI 0.71–1.09) and myocardial infarction (OR 0.90; 95% CI 0.77–1.05) between patients who underwent off-pump CABG (OPCAB) and those who underwent on-pump CABG. However, OPCAB resulted in a lower incidence of cerebral stroke (OR 0.72; 95% CI 0.56–0.92). Furthermore, a significant relationship between patient risk profile and benefits from OPCAB was found for all-cause mortality, myocardial infarction, and cerebral stroke.[76] OPCAB was also associated with less transfusion, shorter intubation time, and reduced length of hospital stay.[1,77]

Several studies have assessed these two techniques in patients with end-stage renal disease. Ariyoshi et al. reported that the morbidity rate was significantly lower in hemodialysis patients undergoing OPCAB (8.3%) versus on-pump CABG (47.8%).[62] Perioperative mortality was 0% in the OPCAB group and hospital stay was shorter for patients undergoing OPCAB (9.7 vs. 28.5 days, respectively).[62] A total of 13,085 patients on dialysis were identified from the USRDS database, of which 2,335 (17.8%) underwent OPCAB surgery. There was no significant difference in in-hospital mortality rate (OPCAB: 9.7% vs. on-pump CABG: 11.0%) and cardiac mortality during the follow-up period (23.6% vs. 23.8%, respectively; adjusted HR 0.95; 95% CI 0.86–1.04). Moreover, OPCAB was associated with reduced all-cause mortality compared to on-pump CABG (HR 0.92; 95% CI 0.86–0.99). However, the observed survival benefit was mostly apparent in the first year after surgery (70.3% vs. 68.7%), but was not main-

tained after 2 years (55.4% vs. 55.2%, respectively).[78] Reports also suggest an improved long-term outcome in patients undergoing on-pump CABG. This may be due to the difference in complete revascularization rate, where on-pump CABG is associated with more anastomoses and a higher rate of complete revascularization (OPCAB: 2.4 ± 1.0 vs. on-pump CABG: 3.3 ± 0.9).[79] The lower incidence of complete revascularization in OPCAB may be crucial for patients with advanced renal disease, who have more aggressive coronary artery disease and a higher rate of progression after surgery.[80] The superiority of OPCAB in long-term outcome has not been proven.[80] However, Horai et al. reported acceptable early and mid-term outcomes in patients on hemodialysis who underwent complete revascularization by OPCAB.[81] In their study, the average anastomoses were 3.7 with an actuarial survival rate of 88.8% and 77.0% at 1 and 3 years, respectively. Early graft patency was 98.8%. Low ejection fraction and history of smoking were identified as risk factors associated with mid-term outcomes.[81]

Several other factors have been identified as predictors for long-term outcomes. These include the use of internal thoracic artery grafts, which was independently associated with improved survival after CABG (HR 0.92; 95% CI 0.87–0.98)[78]; and the use of cardiopulmonary bypass, an independent risk factor for early death (OR13.6; 95% CI 1.7–110) in patients undergoing hemodialysis.[79]

Perioperative management

Patients undergoing hemodialysis are at higher risk of infection such as pneumonia, kidney, and urinary tract infections, bloodstream infections, and cellulitis. In a study of 9,697 patients undergoing hemodialysis, 27.9% of the patients were hospitalized during the median follow-up of 13.6 years due to infection. Of those, patients with a lower estimated glomerular filtration rate (eGFR) were at higher risk of infection-related death (eGFR 15–29 ml/min/1.73m^2: HR 3.76, 95% CI 1.48–9.58; eGFR 30–59 ml/min/1.73m^2: HR 1.62, 95% CI 1.20–2.19; eGFR 60–89 ml/min/1.73m^2: HR 0.99, 95% CI 0.80–1.21).[82] Mesenteric ischemia is another risk factor for patients undergoing dialysis. Non-occlusive mesenteric ischemia accounts for approximately 20–30% of all mesenteric ischemia cases and is associated with a mortality rate of up to 50%. Risk factors include advanced age, myocardial infarction, congestive heart failure, aortic insufficiency, renal or hepatic disease, and cardiac surgery. Patients undergoing hemodialysis develop non-occlusive mesenteric ischemia at an increased rate, especially in patients with episodes of hypotension.[83] Excessive ultrafiltration or an excessively rapid filtration rate may induce ischemia in these patients. Therefore, fluid management is essential for the prevention of non-occlusive mesenteric ischemia.[84] Vasospasm of the mesenteric artery is diagnosed by selective angiography, and direct intra-arterial vasodilator therapy is the only known effective treatment.[85]

Hemodialysis access has also been shown to affect cardiac function. A study comparing 60 patients with arteriovenous access and 43 patients with double-lumen tunneled cuffed central venous catheter reported that more patients with arteriovenous access experienced heart failure (OR 5.1) during a median follow-up period of 27.6 month.[86] Selection of vascular access may be another option for the reduction of cardiac event risk in uremic patients.

Conclusion

Advances in medical therapy extend the lives of patients despite the high prevalence of comorbidities associated with advanced age and cardiovascular events. More high-risk patients are referred for surgery, including patients undergoing hemodialysis who require coronary revascularization. Complete revascularization with minimally invasive methods, coupled with optimal medical therapy for the treatment of the underlying vascular pathology are necessary to improve outcomes in patients with end-stage renal disease.

Disclosure Statement

All authors have no conflict of interest.

Author Contributions

Study conception: DH, AY, HA
Data collection: DH, AY
Investigation: DH, AY
Writing: DH, AY, HA
Critical review and revision: all authors
Final approval of the article: all authors
Accountability for all aspects of the work: all authors

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