Chapter 1

Cardiovascular Disease in Hemodialysis Patients

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1. Introduction

Cardiovascular disease (CVD) is a most common complication and a chief cause of death in patients with end stage renal disease (ESRD) accounting for 45% to 50% of causes of death in ESRD patients. In ESRD patients, mortality due to CVD is 10~30 times higher than in the general population. 80% patients on maintenance homodialysis (MHD) had cardiovascular complication. In Chinese patients, the prevalence of CVD in young MHD patients was as high as 63.8%, and its characteristics were similar to middle- and old-aged MHD patients. This is likely due to ventricular hypertrophy as well as nontraditional risk factors, such as chronic volume overload, anemia, inflammation, oxidant stress, homocysteine and other aspects of the uremic milieu. China collaborative study on dialysis: a multi-centers cohort study on cardiovascular diseases in patients on maintenance dialysis showed that cardiovascular morbidity during chronic dialysis was more prevalent in peritoneal dialysis (PD) than HD patients among those with old age and long-term dialysis. Metabolic disturbance-related risk factors were independently associated with CVD only in PD patients. Better understanding the impact of dialysis modality on CVD would be an important step for prevention and treatment [1]. In this chapter we focus on epidemiology and management of traditional and nontraditional CVD risk fators and on ischemic heart disease, heart failure and arrhythmia.

2. Traditional risk factors

2.1. Hypertension

2.1.1. Epidemiology and pathophysiology

Hypertension is a common complication in patients with chronic kidney disease. The incidence of hypertension grows along with the decrease in glomerular filtration rate (GFR). It

was reported that the incidence of hypertension in patients with GFR less than 60 ml/min was 50%-75%. However, the incidence of hypertension was extraordinarily higher in MHD patients. In 69 dialysis units in the United States, almost 86% of MHD patients were suffering from hypertension, and the control rate for their BP was merely 30%[2]. Hypertension is a significant risk factor for cardiovascular disease in MHD patients. Foley et al [3] found that with each 10 mm Hg increase of BP in MHD patients, the risk of LVH increased by 48%, ischemic heart disease increased by 39% and congestive cardiac failure increased by 44%.

The causes of hypertension in MHD patients are miscellaneous, including volume overload [4], activation of the RAS [5], sympathetic hyperactivity [6] and increases in inhibitors of nitric oxide (NO) in the blood circulation, such as ADMA [7]- which result in a high incidence of hypertension and difficulties in BP control. MHD patients always need to be treated with combinations of 3 or more categories of antihypertensive drugs.

2.1.2. Definition and drug therapy

a. Definition: Predialysis systolic pressure >140mmHg and/or diastolic pressure >90mmHg when the patient is believed to be at so-called "dry weight".

b. Drug Therapy goal: Arterial pressure goals should be established individually, taking into account age, comorbid conditions, cardiac function, and neurologic status. In patients with raised systolic and diastolic pressure and few background cardiovascular complications, a reasonable predialysis BP goal is <130/80mmHg, that targeted by JNC7 for patients with chronic renal disease. In patients with isolated systolic hypertension and wide pulse pressure (usually elderly patients with atherosclerotic complications), excessive lowering of BP may be hazardous. For them a target predialysis systolic pressure of about 140-150mmHg is prudent.

2.1.3. Treatment

a. Sodium and fluid restricton. Most fluid ingestion is driven by salt ingeston. Sodium restriction of 2g per day(87mmol) should not be onerous, and of the patient is open to a more stringent sodium restriction and caloric and protein intake seem adequate, then this should be encouraged.

b. Longer and/or more frequent/longer dialysis sessions. In some ESRD patients, a regular dialysis schedule, three times per week using 4-hour session lengths will be insufficient to maintain euvolemia. In such patients, the choics are to increase the dialysis session length, or to switch to a four times per week, or even daily dialysis[8].

c. Antihypertensive drug use

The regular antihypertensive drugs in MHD patients include angiotensin-converting enzyme inhibitor (ACEI) or angiotensin receptor blocker (ARB), calcium channel blocker (CCB) and β-receptor blocker or α-receptor blocker. The Avoiding Cardiovascular Events through Combination Therapy in Patients Living with Systolic Hypertension (ACCOMPLISH) trial showed that initial antihypertensive therapy with benazepril plus amlodipine was superior to benazepril plus hydrochlorothiazide in reducing cardiovascular morbidity and mortality.

The ACCOMPLISH trial [9] was a 3-year multicenter, event-driven trial involving patients with high cardiovascular risk who were randomized in a double-blinded manner to benazepril plus either hydrochlorothiazide or amlodipine and titrated in parallel to reach recommended blood pressure goals. Of the 8125 participants in the United States, 1414 were of self-described Black ethnicity. The composite kidney disease end point, defined as a doubling in serum creatinine, end-stage renal disease, or death was not different between Black and non-Black patients, although the Blacks were significantly more likely to develop a greater than 50% increase in serum creatinine to a level above 2.6 mg/dl. They found important early differences in the estimated glomerular filtration rate (eGFR) due to acute hemodynamic effects, indicating that benazepril plus amlodipine was more effective in stabilizing eGFR compared to benazepril plus hydrochlorothiazide in non-Blacks. There was no difference in the mean eGFR loss in Blacks between therapies. Thus, benazepril coupled to amlodipine was a more effective antihypertensive treatment than when coupled to hydrochlorothiazide in non-Black patients to reduced kidney disease progression. Blacks have a modestly higher increased risk for more advanced increases in serum creatinine than non-Blacks.

A recent research in China showed that the nitrate can decrease BP, reduce the total categories and quantities of other antihypertensive drugs needed, reverse LVH modeling and reduce the rate of acute heart failure in MHD patients, with good tolerance and safety, by the release of NO which is probably antagonized by ADMA in ESRD subjects. It is, therefore, appropriate to consider sustained-release nitrates as the sixth category of antihypertensive drugs for MHD patients, in addition to ACEIs and ARBs, CCBs, β-receptor blockers and α-receptor blockers [10].

2.2. Smoking

Smoking is associated with progression early-stage CKD patients, and may well adversely impact residual renal function in dialysis patients [11]. Smoking strongly associates with incident heart failure, incident peripheral vascular disease, and all-cause mortality in the U.S. Renal Data System (USRDS). Post hoc analysis of the HEMO Study in patients with available comorbidity, clinical, and nutritional data. The results showed that 17% were current smokers and 32% were former smokers at baseline. After case-mix adjustment, compared with never smoking, current smoking was associated with greater infection-related mortality (hazard ratio [HR], 2.04; 95% confidence interval [CI], 1.32-3.10) and all-cause mortality (HR, 1.44; 95% CI, 1.16-1.79) and greater cardiovascular (incidence rate ratio [IRR], 1.49; 95% CI, 1.22-1.82) and all-cause (IRR, 1.43; 95% CI, 1.24-1.65) hospitalization rates. The population attributable fraction (i.e., fraction of observed deaths that may have been avoided) was 5.3% for current smokers versus never-smokers and 2.1% for current versus former smokers [12].

2.3. Diabetes

Diabetics are at higher risk for acute coronary syndromes. Additionally, there is increased prevalence of heart failure. Poor blood glucose control is associated with increased mortality in dialysis patients [13]. NKF-K/DOQI guidelines recommend a target HbA1c of <7% for patients with DM and CKD[14]. A prospective interventional study in patients with DM but

without renal failure showed an increase in all-cause mortality in patients with HbA1c <6% attained by intensive therapy compared to the standard therapy group[15]. Nonetheless some small observational studies mostly performed in Asian populations indicate the importance of good glycemic control for survival in dialysis patients with DM [16,17,18]. One observational study from Germany found higher HbA1c values to be a risk factor for all-cause mortality and cardiovascular disease[19]. However, in several studies no association between HbA1c and neither patient survival[20,21,22] nor cardiovascular disease [23] could be shown in dialysis patients with DM. Most of these studies were based on a single measurement of HbA1c values. Only two studies considered time-dependent analyses using all available measurements of HbA1c during the whole observation period instead of using only a baseline measurement [24]. Insulin resistance (IR) is highly prevalent in MHD patients and is associated with poor cardiovascular outcomes. Hyperinsulinemic euglycemic glucose clamp (HEGC) is the gold standard for measuring IR. An observational study in USA found that eighty-three percent of the subjects displayed either glucose intolerance or overt insulin resistance by HEGC (GDR median, 5.71; interquartile range [IQR], 4.16, 6.81). LAR and HOMA-AD were the best correlates of IR measured by HEGC (r=-0.72, P<0.001, and -0.67, P<0.001), respectively. Fat percentage, interleukin-6, and adipokines (leptin, adiponectin, and resistin) were strongly associated with GDR. HEGC, LAR, and HOMA-AD had the best intraclass correlation coefficients [25].

2.4. Dyslipidemia.

Dyslipidemia is a well-established metabolic disorder in dialysis patients. A recent study [26] found that a significant increase of serum triglycerides (p= 0.002), lipoprotein (a) (p = 0.001) and C Reactive Protein (p = 0.008) was observed in patients when compared with healthy controls. A significant decrease of serum total cholesterol (p=0.01), HDLcholesterol (p<0.001), LDL-cholesterol (p=0.005) and apolipoprotein AI (p<0.001) was also observed in patients. A study of cholesterol metabolism in patients with hemodialysis in the presence or absence of coronary artery disease showed that HD patients showed lower cholesterol concentrations than non-HD patients, and, as compensation, their cholesterol absorption might be accelerated. However, higher cholesterol synthesis, which was correlated with higher BMI, might be an independent predictor for the presence of coronary artery disease in HD patients [27].

2.4.1. Cholesterol

In dialysis, the relationship of total or low-density lipoprotein (LDL) cholesterol to mootality is U-shaped; patients with LDL cholesterol levels above 100 mg/dL (2.6 mmol/L) are most likely at increased risk for adverse cardiovascular outcomes, but low levels, probably indicating malnutrition, also are associated with higher mortality rates. Despite frequently reduced levels total and LDL cholesterol, atherogenic lipoprotein remnants and lipoprotein (a) are generally increased and high-density lipoprotein (HDL) cholesterol levels are generally reduced, likely contributing to CVD risk. On the other hand, Dialysis per se have neutral effects on serum lipid profile, however, certain dialysis-related parameters may have signifi-

cant affect on lipoprotein metabolism and modify the feature of dyslipidemia in hemodialysis (HD) patients. These parameters include; membrane used in dialyzer (high flux vs. low flux), type of dialyzate (bicarbonate *vs.* acetate), anticoagulant (heparin) and the phosphate-binder (sevelamer hydrochloride). The use of high-flux polysulfone or cellulose triacetate membranous instead of low-flux membrane is associated with a significant reduction in triglyceride levels and an increase in apolipoprotein Al and HDL-cholesterol levels[28].The use of bicarbonate dialyzate may result in higher HDL-cholesterol concentrations than the use of acetate dialysate[29]. Chronic use of heparin as an anticoagulant releases lipoprotein lipase from the endothelial surface which may result in lipoprotein lipase depletion and defective catabolism of triglyceride rich-lipoprotein. Finally sevelamer hydrochloride significantly reduces the concentration of total cholesterol and apolipoprotein-b in HD patients[30].

2.4.2. Hypertriglyceridemia

Nearly one third of dialysis patients have hypertriglyceridemia, defined by levels above 200 mg/dL (2.26 mmollL), with levels occasionally up to 600 mg/dL (6.8 mmol/L). The predominant underling cause is a deficiency of lipoprotein lipase, resulting in reduced lipolysis of triglyceride (TG)-rich very low-density lipoproteins (VLDLs) and yielding high quantities of atherogenic remnant lipoproteins. Enrichment of LDL particles with triglycerides also suggests partial deficiency of hepatic lipase.

2.4.3. Measurement

If possible, dialysis patients should be evaluated with a fasting (although perhaps recommended we know not practical) serum lipid panel that includes total and HDL cholesterol as well as triglycerides.

a. LDL cholesterol. LDL cholesterol is commonly computed by subtracting the serum triglyceride level divided either by 5 (when TGs are measured in mg/dL) or by 2.19 (when TGs are measured in mmol/L) as well as the HDL cholesterol level from the total cholesterol.

b. Atherogenic, remnant lipoproteins and non-HDL cholesterol. In persons without elevated triglyceride levels (TG<200 mg/dL or 2.26 mmol/L), levels of atherogenic remnant lipoproteins correlate well with the calculated LDL cholesterol. When 200 <TG <500 mg/dL (2.26 <TG <5.64 mmol/L), levels of atherogenic remnant lipoproteins correlate well with VLDL levels.

2.4.4. Treatment

a. Target lipid levels. Because dialysis patients the highest risk group for CVD events, current KDOQI guidelines recommend that dyslipidemia shouldbe more aggressively treated than in the general population, with an LDL cholesterol target level below 100 mg/dL (2.6 mmol/L). Even lower LDL targets (70 mg/dL or 1.8 mmol/L) have been advocated in diabetic patients during the earlier stages of CKD based on extrapolation

from resuIts in nonuremic individuals. However, there is no direct trial evidence to support these lower LDL targets in diabetic patients with any srage of CKD. Treatment of very high TG levels (>500 mg/dl or 5.7 mmol/L) is recommended to protect against TG pancreatitis.

b. Drug (statins) therapy. Statins (HMG-CoA Reductase inhibitor) are the most commonly prescribed agents for the treatment of hypercholesterolemia. Statins primarily inhibit hepatic cholesterol biosynthesis through inhibition of HMG-CoA reductase. The net effect of statins administrations are reduction in serum total cholesterol and LDL-cholesterol, modest reduction in serum TG and modest elevation in serum HDL. Statins have multiple pleiotropic effects beside their significant cholesterol lowering effect. They include; reduction of proteinuria in human[31], anti-inflammatory effect and reduction of fibrosis of tubular cells. Treatment with HMG-CoA reductase inhibitors is associated with the attenuation of progression of atherosclerosis and reduction in cardiovascular and cerebrovascular events. The beneficial effects of statins are observed at the endothelial level, displayed by atherosclerotic plaque stabilization and in some case plaque regression[32]. The potential adverse effects associated with statin therapy are important to consider in the management of dyslipidemia in patients with ESRD. An recent study of Heart and Renal Protection showed that reduction of LDL cholesterol with simvastatin 20 mg plus ezetimibe 10 mg daily safely reduced the incidence of major atherosclerotic events in a wide range of patients with advanced chronic kidney disease [33].

3. Nontraditional risk factors

3.1. Chronic volume overload

Volume overload is a common manifestation in MHD patients [34]. Volume overload can increase returned blood volume, cardiac afterload, LVDd/LVEDV, and left ventricle wall pressure [35,36]. In early stage, the cardiac changes of adaptive ventricular chamber enlargement and myocardial hypertrophy induced by volume overload maybe reversible. Removal and control of excess fluid with dialysis is considered critical for protection against cardiovascular sequelae. A recent Chinese study found that antihypertensive agents including beta-blockers may influence hemodynamics, which may limit fluid removal during hemodialysis [37].

3.2. Anemia

Anemia is predictive of morbidity and mortality from cardiovascular causes in patients with CKD or on dialysis [38]. It leads to reduced oxygen delivery to tissues, causing organ dysfunction. It also causes hemodynamic adaptations including a high cardiac output state to maintain adequate tissue oxygenation leading to left ventricular dilatation and hypertrophy [39]. However, at the present time, correction of anemia to hemoglobin levels above 13 g/dL (130 g/L) has not been associated with a cardiovascular or survival benefit. Maintenance of hemoglobin levels above 11 g/dL (110 g/L) is currently recommended and may prevent further progression of LVH. Guidelines for the management of anemia and iron

deficiency in chronic hemodialysis (HD) patients have been developed to standardize therapy and improve clinical outcome. But a recent Dutch study found that compliance with anemia targets in stable HD patients was poor and showed a wide variation between treatment facilities [40].

3.3. Inflammation

The role of chronic inflammation as a putative cause of high mortality in ESRD has attracted considerable interest during the last decade. It has been hypothesized that in addition to its direct pro-atherogenic effects, chronic inflammation may serve as a catalyst and in the toxic uremic milieu may modulate the effects of concurrent vascular and nutritional risk factors [41]. ESRD has become a prototype for chronic inflammation. There is consistent evidence that CRP and pro-inflammatory cytokines such as IL-1, IL-6 and TNF-α are risk factors for atherosclerotic complications and predict death and adverse cardiovascular outcomes in these patients [42,43,44,45]. Schwarz et al. [46] have shown that coronary atherosclerotic plaques in ESRD patients are characterized by increased medial thickness, infiltration by and activation of macrophages and marked calcification. Available evidence suggests that heavily calcified and inflamed plaques contribute to excessive cardiovascular risk in ESRD patients [47]. Levels of CRP increase as the renal function deteriorates and are particularly high in patients with ESRD. As many as one third to one half of patients with ESRD have CRP levels in the very high-risk category, and CRP continues to be an excellent predictor of adverse outcome in this population [48]. Parekh et al. [49] prospectively studied a cohort of more than 1,000 ESRD patients followed for a median of 2.5 years and reported that the highest tertile of CRP was associated with a two-fold increased adjusted risk of sudden cardiac death compared to patients in the lowest tertile.

3.4. Oxidant stress

Numerous factors in the dialysis patient increase o xidative stress (OxStress). These include inflammation (as marked by elevated C-reactive protein), malnutrition (by reducing antioxidant defenses), uremic toxins, and, potentially, the dialysis procedure itself. Many protective mechanisms are impaired, including reduced plasma protein-associated free thiols such as glutathione. This may magnify the impact of OxStress in the dialysis population. OxStress is recognized as a critical factor in the development of atherosclerotic cardiovascular disease (ACVD) [50,51]. According to the oxidation hypothesis of atherosclerosis, low-density lipoprotein (LDL) in its native state is not atherogenic [52,53]. LDL must undergo oxidative modification before it can contribute to the initiation and progression of atherosclerosis. Data from animal models of atherosclerosis, both diet-induced and genetically altered models, have demonstrated the presence of oxidized LDL (oxLDL) in plasma as well as in atherosclerotic lesions. Presence of oxLDL, autoantibodies against malondialdehyde-modified LDL, and of LDL-IgG immune complexes has also been reported in human plasma and human atherosclerotic lesions [54,55]. The pathways involved in the formation of these oxidative markers and the relationship between these markers and disease progression remain to

be elucidated. Advanced oxidation protein products (AOPP) accumulation is a marker of oxidative stress. A recent study in China [56] found that accumulation of AOPP was more significant in HD compared to CAPD patients. The level of AOPP was independently associated with ischaemic heart disease only in HD patients.

3.5. Hyperhomocysteinemia

3.5.1. Epidemiology

Hyperhomocysteinemia is much more common in dialysis patients than in the general population. Homocysteine is typically measured in the plasma and normal levels range between 5 and 12 mcmol/L. In the general population, hyperhomocysteinemia is an independent risk factor for adverse CVD outcomes and is commonly associated with deficiencies in folate and vitamins B_6 and B_{12}. B-vitamin and folate supplementation effectively reduce homocysteine levels in the general population and recent extensive folate supplementation in foods has lowered the overall prevalence of hyperhomocysteinemia in the nondialysis population. Homocysteine levels increase dramatically as kidney function declines, with as many as 80% of dialysis patients classified as having hyperhomocysteinemia. In dialysis patients, some but not all studies suggest that hyperhomocysteinemia is independently associated with CVD mortality. Nutritional status confounds these analyses, since better nourished patients tend to have higher homocysteine levels. The relationship between homocysteine levels and cardiovascular disease was described initially by observational studies, which may overestimate the effect of this relationship. Two meta-analyses of epidemiologic studies [57,58] suggested that reduced homocysteine levels could lower the risk of coronary heart disease, stroke, and cardiovascular disease. However, Bazzano et al [59] concluded that folic acid therapy did not significantly contribute to cardiovascular disease, stroke, or myocardial infarction.

3.5.2. Treatment

Folic acid supplementation may play an important role in carcinogenesis, because when it is administered to individuals with established cancers, it potentially promotes tumor growth [60,61]. It has also been reported that the introduction of folic acid may increase the risk of colorectal cancer [62]. According to our review, folic acid therapy resulted in an 8% increase in the risk of cancer, although this difference was not statistically significant. The reason for this increase in carcinogenesis can be explained by the fact that folic acid supplementation may affect endothelial function and support cell growth through mechanisms independent of homocysteine [63]. Importantly, folic acid and B vitamins are water-soluble and excreted by the kidney; therefore, therapy toxicity may be of great concern in patients with impaired renal function. In patients with end-stage renal failure who have hyperhomocysteinemia wherein homocysteine levels must be reduced, alternative, non-vitamin therapies are important. For example, enhancing urinary excretion can help to avoid a decrease in glomerular filtration rate and an increase in major cardiovascular events [64].

4. Ischemic heart disease

4.1. Epidemiology

Acute myocardial infarction(AMI) is common in the ESRD population. Outcomes for patients with AMI are poor, with 50% 1-year mortality. Both atherosclerosis and atheriosclerosis and arteriosclerosis contribute to pathogenesis; arteriosclerosis may cause LVH with increased myocardial oxygen demand and altered coronary perfusion with subsequent subendocardial ischemia.

4.2. Diagnosis

Routine screening is not currently recommended. There are no preoperative screening guidelines specific to dialysis patients, and it is reasonable to use general population guidelines, recognizing that the extent of comorbid conditions prevalent in the dialysis population is Iikely to place them into the highest cardiovascular risk group. Because many dialysis patients are unable to achieve adequate exercise levels for valid stress tests, pharmacologic stress test should be used in this population. Furthermore, because of the high incidence of baseline electrocardiogram abnormalities, either nuclear or echocardiographic imaging should be utilized in stress testing.

4.3. Prevention

Aspirin, beta-blockers, ACE inhibitors, and nitrate preparations are all appropriate for primary therapy of AMI and are likely appropriate for secondary prevention, although data on aspirin for secondary prevention of coronary artery disease remain inadequate to date. Observational studies suggest that medical therapies including aspirin, beta- blockers, and ACE inhibitors may be underutilized in dialysis patients. Using the ESRD database and the Cooperative Cardiovascular Project (CCP) database, Berger AK, et al [65]found that ESRD patients are far less likely than non-ESRD patients to be treated with aspirin, beta-blockers, and ACE inhibitors during an admission for AMI. The lower rates of usage for these medications, particularly aspirin, may contribute to the increased 30-day mortality.

4.4. Treatment

4.4.1. Management of angina pectoris

The pharmacologic approach to angina in dialysis patients is similar to that in the general population. The progressive introduction of sublingual nitrates, oral long-acting nitrates, beta-blockers, and calcium channel blockers is appropriate. The usual dosages of sublingual and oral nitrates can be given to dialysis patients.

4.4.2. Angina during the hemodialysis session

For patients whose angina manifests primarily during hemodialysis session, a number of therapeutic options available. Nasal oxygen should be given routinely. If the anginal episode is associated with hypotension, then initial treatment should include raising the blood pressure by elevating the feet and by cautiously administering saline. Sublingual nitroglycerin can be given as soon as the pressure has increased to a clinically acceptable value. Consideration should be given to reducing the blood flow rate and stopping ultrafiltration until the anginal episode subsides. Predialysis administration of 2% nitroglycerin ointment may be of benefit when applied 1 hour prior to a hemodialysis session, assuming that the blood pressure will tolerate this intervention.

5. Heart failure

Heart failure is the commonest manifestation of cardiac dysfunction in patients on maintenance dialysis. According to the cross-sectional survey by Harnett and coworkers, which included both hemodialysis and peritoneal dialysis patients, nearly one-third of the patients developed heart failure on initiation of dialysis, of which 56% had further recurrences [66]. Even among patients with no heart failure at baseline, around 25% of patients developed heart failure at a rate of 7% per year. In addition, the presence of heart failure was associated with a worse prognosis in that median survival was 36 months for patients with heart failure at baseline compared to 62 months for patients without heart failure. They also found that increasing age, diabetes mellitus and ischemic heart disease were associated with heart failure at initiation of dialysis, while ischemic heart disease, anemia, hypoalbuminemia and systolic dysfunction were important predictors of heart failure recurrence [67]. The presence of ischemic heart disease is associated with greater left atrial diameter, greater left ventricular end-systolic diameter, lower fractional shortening and, thus, more systolic dysfunction [68].In the Canadian Prospective Cohort Study, which included 433 incident dialysis patients, 74% had left ventricular hypertrophy at baseline, 30% had left ventricular hypertrophy with dilatation, and 15% had systolic dysfunction [69], indicating that much of the cardiac hypertrophy and dysfunction was already established by the time patients started their dialysis therapy. This may also explain why dialysis patients are prone to develop heart failure.

6. Arrhythmia

Paroxysmal atrial fibrillation attack is one of most common tachyarrhythmia in MHD patients. Paroxysmal atrial fibrillation attack not only can affect the dialysis to proceed smoothly, but also it can increase the death risk in MHD patients. In the Dialysis Outcomes and Practice Patterns Study [70], which analyzed 37,765 participants in 12 countries in the Dialysis Outcomes and Practice Patterns Study to explore the association of the following

practices with sudden death (due to cardiac arrhythmia, cardiac arrest, and/or hyperkalemia): treatment time [TT] <210 minutes, Kt/V <1.2, ultrafiltration volume >5.7% of postdialysis weight, low dialysate potassium [K(D) <3 mEq/L]), and prescription of Q wave/T wave interval-prolonging drugs,indicating that identified modifiable dialysis practices associated with higher risk of sudden death, including short TT, large ultrafiltration volume, and low K(D). Because K(D) <3 mEq/L is common and easy to change, K(D) tailoring may prevent some sudden deaths. Individualized interventions may effectively reduce paroxysmal atrial fibrillation attack during dialysis in MHD patients. The general individualized intervention in MHD patients are, (1) individualized dialysis programmes, such as increasing the dialysis or hemodialysisfiltrition frequency or be changed to daily dialysis for atrial fibrillation with frequent seizure. Regular monitoring of serum potassium levels before and post dialysis, adjusting dialysate concentration of potassium ions in a timely manner, using different prescription of individualized dialysate for hemodialysis treatment. (2)Behavioral interventions, such as improving their way of life to develop good habits and patterns of dialysis. (3) Closely monitoring the patients' vital signs during hemodialysis, such as heart rate, blood pressure and pulse rate. (4) Controlling interdialytic weight gain (IDWG), strict volume policy including salt restriction and adequate ultrafiltration is fundamental to reach normovolemia/normotension together with regression of left atrial hypertrophy in patients on hemodialysis. In HD patients, IDWG is significantly associated with left atrial volume/diameter. Together with better volume control, left atrium volume must be decreased. Most importantly, they should focus on salt restriction not water restriction. (5) Psychological intervention to reduce sympathetic excitement to induce atrial fibrillation.

7. Conclusion

A high prevalence of cardiovascular disease is observed in ESRD patients receiving dialysis therapy. This usually constitutes a combination of vascular and myocardial disease related to both traditional and nontraditional risk factors. Most of these cardiovascular complications are already established and advanced by the time patients are started on dialysis treatment, thus indicating the need for earlier and more active screening for cardiovascular disease even before patients progress to end-stage kidney disease. More attention should be focused on improving cardiovascular outcomes in ESRD patients receiving maintenance dialysis therapy.

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