Cardiovascular problems in ESRD patients

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Only the most recent references updating the chapter will be included in this manuscript.

INTRODUCTION

Cardiovascular disease (CVD) exerts a major influence on the morbidity and mortality of dialysis patients, as demonstrated by the frequent occurrence of heart failure and ischemic heart disease, very high mortality rates, and high proportion of cardiac deaths. These adverse events can usually be attributed to disorders of cardiac muscle structure and function and/or disorders of perfusion. Hemodynamic, metabolic and other risk factors are prevalent in dialysis patients which predispose to various cardiac disorders, some of which may be amenable to intervention.

EPIDEMIOLOGY

The epidemiology of cardiovascular disease in ESRD patients, mostly based on North American data has recently been summarized[1,2].

Mortality: Based on European data, there is a relatively constant 16- to 19-fold higher death rate in patients with ESRD as compared with the general population.

Recent epidemiological data from the USA also show that cardiovascular mortality defined by death due to arrhythmia's, cardiomyopathy, cardiac arrest, myocardial infarction, atherosclerotic heart disease, and pulmonary edema is significantly higher in each age category in ESRD patients compared to the general population.

Thus the increased mortality from cardiovascular disease appears to relate to the presence of ESRD and additional factors such as diabetes superimposed on underlying fundamental genetic and/or environmental differences in susceptibility to cardiovascular disease in different populations.

Hemo vs *peritoneal dialysis:* Until now, no randomized conrolled studies of PD versus HD have been performed, and thus no hard data favoring one dialysis method over another is at present available. There is however enough evidence in the present literature to claim that survival outcomes in PD and HD are at least comparable in centers experienced in both methods. Recent data obtained in Canada suggest that survival in the first 2-3 years after start of RRT might even be better in PD.

Mortality data suggest that like in hemodialysis, cardiovascular disease is by far the most common cause of death in PD patients. Also in the recent CANUSA study on adequacy and nutrition in CAPD patients, 75% of the deaths during the two year study period were cardiovascular in nature.

Morbidity: A large cohort (N = 496) of new Canadian hemodialysis patients were followed for a mean of 218 days. During this period there were 30 ischemic events (myocardial infarction or angina) requiring hospitalization, giving a probability of 8% per year, and there were 40 episodes of pulmonary edema requiring hospitalization or additional ultrafiltration, giving a probability of 10% per year. In a group of 31 PD patients only 15 had no evidence of ischemic heart disease. De novo appearance of ischemic heart disease in CAPD patients has been reported to be 8.8% after one year and 15% after 2 years.

The prevalence of coronary heart disease, congestive heart failure, and left ventricular hypertrophy is similar in PD and HD patients[1,2].

Among incident hemodialysis patients, 42% had a history of coronary heart disease, and 40% had a history of congestive heart failure. Among peritoneal dialysis patients, 36% had coronary heart disease, while 31% had congestive heart failure.

However, only 13% of the 42% hemodialysis patients with coronary heart disease had either angioplasty or abnormal coronary angiography; therefore a large percentage were classified as having coronary heart disease on the basis of ill-defined criteria. It is thus possible that even these high preva-

lences of cardiovascular diseases are underestimations of the true prevalence. Also in the US, as yet unpublished data suggest that approximately one-third of first hospitalizations are secundary to CVD, which is roughly equivalent to an incidence of 40 first hospitalizations per 100 patient-years[2].

PATHOGENESIS

The pathogenesis of cardiovascular disease in ESRD patients has been recently reviewed by Amann and Ritz[3], Parfrey[4], and London y et al[5].

Myocardial disease

Maintenance of normal LV wall stress necessitates the development of LV hypertrophy if LV pressure rises or LV diameter increases, which is initially a beneficial adaptive response.

However, continuing LV overload leads to maladaptive myocyte changes and myocyte death, which may be further exacerbated by diminished perfusion, malnutrition, uremia, and hyperparathyroidism. This loss of myocytes will predispose to LV dilatation and ultimately systolic dysfunction. In addition myocardial fibrosis occurs, which will not only diminish cardiac compliance, but attenuate the hypertrophic response to pressure overload.

Disorders of left ventricular (LV) structure include concentric LV hypertrophy, a response to LV pressure overload, and LV dilation with hypertrophy, a response to LV volume overload. These structural abnormalities predispose to diastolic dysfunction, in which diminished compliance results in a higher than normal change in LV pressure for a given change in LV volume. Ultimately failure of the pump function of the heart (systolic dysfunction) occurs. Both diastolic and systolic dysfunction predispose to symptomatic left ventricular failure. Hemodialysis patients provide the quintessential model for overload cardiomyopathy, because LV pressure overload occurs frequently from hypertension and occasionally from aortic stenosis, and LV volume overload is ubiquitous due to the presence of an arteriovenous fistula, anemia and hypervolemia.

The ill effects of hypertension have been attributed to a reduction in the calibre or the number of arterioles, resulting in increased peripehral resistance. This definition does not take into account that blood pressure fluctuates during the cardiac cycle and that systolic and diastolic blood pressures are merely the limits of this oscillation. By using Fourier analysis, the blood pressure curve can be decomposed into its steady and oscillatory components. The steady component, that is, mean blood pressure, is determined exclusively by cardiac output and total peripheral resistance, while the oscillatory component (oscillation around this mean) is the pulse pressure that is determined by the pattern of LV ejection, the viscoelastic properties of large conduit arteries (arterial distensibility), and the intensity and timing of the arterial wave reflections. Therefore, pressure overload may be primarily related to increased peripheral resistance (with increased diastolic and mean pressure) or to decreased arterial distensibility and early return of arterial wave reflections (with increased systolic pressure and wide pulse pressure)[6].

Several determinants of systolic and pulse pressure are altered in ESRD patients, including decreased arterial compliance and an early return of arterial wave reflections, which are independent factors associated with the extent of LVH. Decreased arterial compliance and functional alterations observed in ESRD are associated with remodeling of conduit arteries, characterized by arterial dilatation and intima-media hypertrophy. These arterial changes resemble those that occur with aging, such as *arteriosclerosis,* which is primarily medial, characterized by diffuse dilatation and stiffening of major arteries, and must be distinguished from *atherosclerosis,* which is focal, nonuniformly distributed, primarily intimal, inducing occlusive lesions and compensatory focal enlargement of arterial diameters.

The consequences of structural and functional changes of the arterial system in uremic patients is increased pulsatile work of the heart, which accounts in part for the development of parallel LV and vascular adaptation in chronic uremia.

Disorders of perfusion: Coronary artery disease is the usual cause of symptoms of ischemic heart disease in dialysis patients. However non-atherosclerotic disease, resulting from small vessel disease, and/or from the underlying cardiomyopathy, may account for a substantial minority of cases of symptomatic ischemic heart disease. Multiple factors contribute to the vascular pathology of chronic uremia, including chronic injury to the vessel wall, prothrombotic factors, lipoprotein interactions, proliferation of smooth muscle, increased oxidant stress, diminished antioxidant stress, hyperhomocysteinemia, hypertension, diabetes and smoking.

CARDIAC STRUCTURE AND FUNCTION

Prevalence: On echocardiography, of 432 dialysis patients in the Canadian cohort, 41% had concentric LV hypertrophy, 28% LV dilatation, and 16%

had systolic dysfunction on starting dialysis. This implies that causes of LV dysfunction occur in the predialysis phase of chronic renal failure. Two hundred and seventy five patients had a follow up echocardiogram 17 months after starting dialysis therapy. Now the proportion of those who had a normal echocardiogram was 13%, the proportion with concentric LV hypertrophy was 40%, with LV dilatation 26%, and systolic dysfunction 20%. In a subgroup of dialysis patients with normal echocardiogram on starting dialysis (N = 30), 32% had developed concentric LV hypertrophy, 16% LV dilatation and 3% systolic dysfunction in the second year after starting dialysis. In peritoneal dialysis one might accept that blood flow would not increase as much as in hemodialysis patients, because there is no vascular access and less variable fluctuations in salt and water status. In 70 patients treated exclusively with peritoneal dialysis LV cavity volume decreased by 5 ml/m^2 during 1 year's follow-up. When compared to hemodialysis patients the differences in the changes in LV volume approached statistical significance ($p = 0.06$).

In a study of 55 normotensive CAPD patients, the majority of patients with left ventricular hypertrophy had the asymmetric, septal form of left ventricular hypertrophy. The direct correlation between left atrial diameer and left ventricular muscle mass suggests impaired left ventricle diastolic filling. After initiation of CAPD therapy, regression as well as progression in left ventricular hypertrophy has been described.

Echocardiographic disorders of the left ventricle predispose to cardiac failure and to earlier death. One and two year survival rates of 90 and 64% has been reported in systolic dysfunction patients treated with CAPD.

RISK FACTORS FOR CARDIAC DISEASE

Circumstantial evidence and longitudinal studies support several risk factors as important for the development of cardiac disease, but thre are no clinical trials which have demonstrated that any risk factor intervention leads to clinical benefit in dialysis patients.

Many of these risk factors, including anemia[7], dyslipidemia[8], oxidative stress[9], abnormalities in parathormone and divalent ion metabolism[10], hyperhomocysteinemia[11], interactive factors between hemodialysis adequacy and nutrition[12], and thrombogenic factors[13] have been recently summarized.

Only some of these factors will be briefly discussed here.

The risk factors can be categorized as hemodynamic, metabolic, or other.

Cardiovascular risk at onset of dialysis: It is remarkable that the high rate of cardiovascular morbidity and mortality in ESRD patients is occurring at a time when the prevalence of coronary artery disease is declining in the general population. This discrepancy is in part due to the demographics of patients about to be started on dialysis: about one-third are diabetic; the average age is now over 60 years and approximately 16 percent are over 74 years, and many patients have underlying cardiac disease.

In all above-mentioned studies, except one where the morbidity and mortality of PD and HD patients have been compared, cardiovascular, cerebrovascular and peripheral vascular comorbidity at the start of dialysis was associated with increased relative risk of death in both dialysis modalities.

Studies in Gent and Brescia have shown that whereas the survival at 1 year was not influenced by the number of risk factors, patients with 7 to 8 risk factors already showed a statistically lower survival in the second year compared to the other groups. When patients with 5 or more risk factors are considered, their survival is significantly lower from the 4th year on of treatment with CAPD.

Mode of dialysis therapy: Dialysis provides inadequate treatment of the uremic state, but the target quantity of dialysis, which may limit the contribution of «uremic toxins» to cardiac dysfunction, is unknown.

In the Canadian studies, the hemodynamic benefit of peritoneal dialysis did not translate into increased survival. In fact hemodialysis had a late survival advantage over peritoneal dialysis because of the adverse impact of hypoalbuminemia in the latter group. Mean serum albumin in peritoneal dialysis patients in the first 2 years of therapy accounted for 65% of the increase in subsequent mortality. It appears thus that the path to cardiac death is different for hemodialysis and peritoneal dialysis patients. Thus in hemodialysis patients a higher proportion developed cardiac failure, which was associated with hypertension and anemia, and which predisposed to cardiac death. In peritoneal dialysis patients mortality was associated predominantly with hypoalbuminemia, which predisposed to death in unknown fashion.

HEMODYNAMIC RISK FACTORS

Volume overload: In comparison with age, sex, and blood pressure matched nonuremic controls, the LV diastolic diameter is increased in ESRD patients.

The ventricular enlargement is probably attributable to chronic volume/flow overload and high-output state, associated with three factors: 1) salt and water retention; 2) arteriovenous shunts, and 3) anemia. It also may occur in response to myocyte death.

Salt and water retention: a direct relationship between blood volume and LV diameter has been shown. Furthermore, body fluid volume contraction during a dialysis session induces a decrease in the LV diameter and there is a direct correlation between the interdialytic body weight changes and LV volume or LV mass.

It is believed that peritoneal dialysis, because it is a continuous process, is better at controlling salt and water overload than hemodialysis. However many CAPD patients are actually fluid overloaded. Some hemodynamic studies performed at the moment of renal transplantation of CAPD patients show that they are constantly overhydrated. A hyperpermeable membrane with high peritoneal solute transport is a risk factor for this complication.

In addition, the disappearance of the residual renal function has not only a negative impact on the adequacy of peritoneal dialysis but may contribute to the volume overload of the patient in case of poor peritoneal ultrafiltration.

Arteriovenous shunts: Cardiomegaly with high-output cardiac insufficiency may occur as a complication of high-flow A-V shunts, and cardiac function may return to normal after surgical correction.

Anemia: Even in the absence of intrinsic heart disease anemia, could result in high-output heart failure that is induced by vasodilatation and low blood viscosity, with decreased peripheral resistances and increased venous return. In ESRD patients, an association between LV dilatation and anemia has been observed and it was independently associated with the development of de novo cardiac failure, as well as overal mortality.

The studies examining the effect of partial correction of anemia with rHuEpo on echocardiographic abnormalities have consistently shown that treating anemia leads to a decrease in hypoxic vasodilatation, an increased peripheral resistance, reduced cardiac output, and partial reversal of LV dilatation and hypertrophy.

The most recent large multicenter studies on the relationship between the degree of correction of the anemia and outcome have yielded conflicting results.

The Normal Hematocrit Cardiac Trial in the US[14] studied dialysis patients with clinically manifest cardiac disease and who were randomly assigned to targets of partial correction or full normalization of hematocrit.

The study was terminated early because of an increased occurrence of death or nonfatal myocardial infarction and a highly significant increase in loss of vascular access in patients randomly assigned to the normal hematocrit group.

The Canadian randomized trial[15] used similar hemoglobin targets in hemodialysis patients with asymptomatic left ventricular hypertrophy or left ventricular dilatation. Preliminary analysis suggests that full correction can prevent the progression to left ventricular dilatation in those with normal cavity volume, but cannot reverse already established left ventricular hypertrophy or dilatation.

The recent analysis of data obtained in Italy by the Lombardy Registry[16] revealed that a negative correlation between hematocrit and cardiovascular mortality and morbidity exists, and that the outcome was best in the group of patients who had a normal hematocrit.

Hypertension: In cross-sectional studies of ESRD patients, LVH has a loose relationship to blood pressure, being weakly related to diastolic blood pressure and more closely to systolic and pulse pressures. The independent association of hypertension with concentric hypertrophy, has been reported in dialysis patients: higher mean arterial blood pressure was significantly associated with the presence of concentric LV hypertrophy and also with the change in LV mas index from baseline to follow-up echocardiogram 1 year later, independent of age, diabetes, ischemic heart disease, hemoglobin, and serum albumin levels. For each 10-mm increase in blood pressure, the odds ratio for the presence of concentric LV hypertrophy was 1.48. Approximately 80% of patients are hypertensive at the initiation of hemodialysis. However, the prevalence falls to 25 to 30% by the end of the first year, due largely to volume control.

Early reports documented improved blood pressure control and impressive regression of left ventricular hypertrophy in CAPD patients. This beneficial effect is however transient as the number of patients who need more antihypertensive drug treatment subsequently increases with time. Once the residual renal function is very lowe or absent, blood pressure and volume control becomes more difficult and the patients need a higher number of antihypertensive drugs.

In the Canadian cohort, an inverse relationship between blood pressure levels and mortality was observed, with an (adjusted) increase in mortality of 22% for each 10-mm Hg decrease in the mean arterial blood pressure distribution curve. Conversely, even within this range, rising blood pressure was independently associated with an increase in LV mass

index and cavity volume on follow-up echocardiography, de novo ischemic heart disease, and de novo cardiac failure.

METABOLIC RISK FACTORS

Hypoalbuminemia: Hypoalbuminemia and dialysis intensity have been shown repeatedly to be perhaps the most critical predictors of outcome in ESRD patients. In these studies the relationship between hypoalbuminemia and mortality was especially strong; this observation, coupled with the fact that cardiovascular disease far overshadow any other cause of death in ESRD, suggests that the adverse impact of hypoalbuminemia might be mediated via cardiac disease. Among hemodialysis patients, each 1 g/dL fall in mean serum albumin was independently associated with the development of de novo and recurrent cardiac failure, de novo and recurrent ischemic heart disease, cardiac mortality, and overall mortality. Among peritoneal dialysis patients, hypoalbuminemia was independently associated with progressive LV dilatation on serial echocardiograms, de novo cardiac failure, and overal mortality.

How hypoalbuminemia might lead to coronary artery disease and cardiomyopathy in dialysis patients is a matter of pure speculation given our current knowledge.

Disturbances in divalent ion metabolism and hyperparathyroidism, and abnormalities in the lipid and homocysteine metabolism have been recently reviewed and are beyond the scope of this review[8, 10, 11].

Vitamin E deficiency: Vitamin E deficiency may be atherogenic in the general population and vitamin E could afford protection against cardiovascular disease by its antioxidant properties limiting lipoprotein oxidation, inhibitory effects on platelet adhesion and aggregation and on monocyte adhesion to the endothelial cell, its antiproliferative effects on smooth muscle, and intracellular effects on the monocyte leading to decreased ability to release oxygen radicals and cytokines such as IL-1β. There is however, no difference in the vitamin E content of LDL between patients in the predialysis state, on HD, and treated by CAPD.

Oxidant Stress: The oxidative modification of LDL in the vascular wall may be an important step in atherogenesis, and in uremia oxidant activity can be identified[9] and may result from reduced concentration of endogenous antioxidants and increased oxidant production from ongoing low-grade inflammatory processes. Dysregulation in the balance between proinflammatory cytokines and their inhibitors has been shown, which may contribute to the uremia-related chronic immunoinflammatory disorder (for recent review see 12). The evidence to support the presence of oxidized LDL in dialysis patients is however contradictory.

OTHER RISK FACTORS

Smoking: In the USRDS Special Study of Case Mix Severity, smoking increased mortality by 26% in hemodialysis patients; the independent effect of smoking appears to be especially lethal in diabetics with ESRD, in whom it more than doubles mortality rates. A recent retrospective multicenter case control study has once more emphasized that smoking at least in men with primary disease was a significant independent risk factor for ESRD[17].

Diabetes mellitus: Diabetic nephropathy is the most common cause of ESRD. It is widely recognized that this patient group is at a very high risk of cardiovascular disease. In the Canadian study, diabetes was independently associated with concentric LV hypertrophy on baseline echocardiography, the development of de novo ischemic heart disease, and overall mortality and mortality after 2 years.

Diabetes mellitus is an independent risk factor for the development of coronary artery disease and it has been estimated that about a third of asymptomatic diabetic patients on renal replacement therapy have 50% or more stenosis of at least one coronary artery. This prevalence rises markedly with age. It is probable that the true prevalence of asymptomatic coronary artery disease is much higher when the diabetic-ESRD population is considered in its entirety.

Valvular sclerosis in peritoneal dialysis patients: A high prevalence of mitral valvular sclerosis is noted in peritoneal dialysis patients. The most remarkable and almost constant association found at echocardiography was the presence of left atrial dilatation. In the patients who developed mitral annular calcification only duration of CAPD seemed to favor its appearance. Other risk factors such as severe hyperparathyroidism and/or hypertension with left ventricular hypertrophy could not be found as independent risk factors.

The high frequency of valvular calcifications in peritoneal dialysis patients could be related to the high incidence of adynamic bone disease in these patients. An increased incidence of soft-tissue calcifications and a resurgence of the calciphylaxis syndrome in patients with low-turnover bone disease has been described. The pathophysiologic relevance of this finding is underscored by the presence of a strong association between myocardial calcium content and left ventricular function.

CARDIAC ARRHYTHMIAS

There is a considerable variation in the frequency and severity of arrhythmias during hemodialysis, as well as in the interdialytic period. Because of these factors, there is no consensus on the frequency of arrhythmias in ESRD patients and on their clinical significance. The assessment and interpretation of arrhythmias in these patients is difficult because of the wide variations in fluid, electrolyte and acid base balance, changing load of uremic toxins, and the repeated stress of hemodialysis.

Ischemic heartdisease and left ventricular hypertrophy are the most common predisposing factors in the causation of arrhythmias in the non uremic population.

A recent study in which 27 CAPD patients were compared with 27 hemodialysis patients revealed that severe cardiac arrhythmias occurred in only 4% of CAPD and in 33% of the hemodialysis group. It was the lower frequency of left ventricular hypertrophy in CAPD patients that explained the lower incidence of severe arrhythmias.

SCREENING FOR CARDIOVASCULAR DISEASE

Echocardiography is a safe, accurate and versatile tool for detecting myocardial dysfunction in ESRD patients. Its usefulness might be reduced in dialysis patients by failure to standardize the time at which echocardiography is performed. The test should therefore be undertaken when the patient is euvolemic.

Echocardiography is indicated in dialysis patients with heart failure, because the identification of diastolic dysfunction might preclude treatment with digoxin or vasodilators which induce increased cardiac contractility. It should probably be recommended as a screening tool for asymptomatic manifestations of cardiomyopathy, if targeted treatment of potential risk factors might result. It can be recommended to obtain echocardiograms on starting dialysis therapy and to repeat them if clinical problems develop or at 2 year intervals.

Exercise-based stress tests for coronary artery disease are not useful in patients on dialysis. Very few patients achieve adequate exercise levels, lowering the sensitivity of the test substantially. Thallium-201 myocardial imaging used with pharmacological stressors has a moderate degree of sensitivity for detecting CAD, but the results are variable and the accuracy is reduced in dialysis patients.

Dobutamine stress echocardiography is promising, with perhaps the highest degree of sensitivity in detecting CAD in ESRD patients. It is not, however, available in all centres. Patients with symptomatic ischemic heart disease should be investigated with coronary angiography, if revascularization is considered a reasonable option.

MANAGEMENT

It goes without saying that risk factor intervention should include control of volume overload, hypertension, and partial or complete correction of anemia. As outlined above, the target hemoglogin for erythropoietin therapy is under review.

Calcium channel blockers and ACE inhibitors are commonly prescribed antihypertensive agents in ESRD patients. Several ongoing randomized controled trials are assessing whether long-acting calcium channel blockers are safe.

Even in patients who become dependent on dialysis, an intervention that slows the rate of loss of residual renal function would be highly desirable. Whether ACE inhibitors or calcium channel blockers still have this effect after the onset of dialysis therapy is unknown.

The regression of LV hypertrophy lacks a therapeutic trial to demonstrate its benefits in terms of morbidity and mortality. In essential hypertension with blood pressure lowering the decrease in LV hypertrophy is determined by pretreatment LV mass index, magnitude of blood pressure lowering, duration of therapy and antihypertensive drug class. Rank order for regression of LV hypertrophy was ACE inhibition, calcium channel blockers, and β-blockers. In hemodialysis patients an ACE inhibitor perindopril did induce regression of LV hypertrophy.

Hyperlipidemia: In non-renal patients aggressive lowering of LDL cholesterol delayed progression of atherosclerosis in saphenous vein coronary artery bypass grafts and antidyslipidemic therapy prevented myocardial infarction and death. It remains to be determined whether aggressive therapy of dyslipidemia has an impact on patient outcome in ESRD. Depending on the patient's life expectancy, treatment of hyperlipidemia in those with known coronary artery disease can be recommended. If the patient is likely to survive long enough (e.g. 5 years) to obtain benefit from treatment of mild hyperlipidemia, then perhaps this should be undertaken.

Hyperhomocysteinemia: Administration of folic acid reduced plasma homocysteine levels in patients with chronic renal failure. The efficacy of this approach in preventing atherosclerosis in both HD and PD patients remains to be determined.

Management of heart failure: Angiotensin-converting enzyme (ACE) inhibitors have been clearly

shown to improve symptoms, morbidity, and survival in nonuremic individuals with heart failure. ACE inhibitors are efficacious in the prevention of heart failure in asymptomatic patients whose left ventricular ejection fraction is less than 35%, and in patients after myocardial infarction with an ejection fraction of 40% or less. It seems reasonable to extrapolate these results to the dialysis population and to recommed their use in patients with diastolic and systolic dysfunction. A word of caution on the use of ACE inhibitors in heart failure is needed. ACE inhibitors by reducing both the systemic and intraadrenal formation of angiotensin II, thereby removing the stimulatory effect of this hormone on adrenal aldosterone release can induce or aggravate hyperkalemia in dialysis patients.

The use of digoxin and vasodilators is probably different for those with systolic and diastolic dysfunction. Digoxin should probably be prescribed in those dialysis patients with heart failure who have systolic dysfunction (with or without atrial fibrillation). On the other hand, it should be avoided in dialysis patients with normal systolic function and heart failure, because the increased contractility induced by digoxin could worsen diastolic function.

No data exist concerning the efficacy of drug therapy in heart failure in dialysis patients, despite the fact that the etiology of heart failure is different from that in non-renal patients.

Coronary artery revascularization: Dialysis patients fulfilling the anatomic criteria used in the general population are likely to benefit form coronary revascularization. Generally accepted criteria are: 1) one-, two-, or three-vessel disease with angina refractory to medical management, when the intent is to relieve symptoms; 2) left main coronary artery disease; and 3) triple-vessel disease associated with ventricular dysfunction or easily inducible ischemia, when the intent is to improve survival. Coronary artery bypass surgery appears to be an effective means of relieving chest pain in patients with ESRD. The surgical mortality was 9%, which is higher than the 3% mortality observed in non-renal patients. This may relate more to the level of LV function than to other factors associated with ESRD.

Although the data on outcome of coronary artery bypass surgery in ESRD are limited, there is even less information on angioplasty outcomes. If surgery is chosen in symptomatic patients, it is associated with greater initial morbidity than angioplasty, but is more effective in the relief of angina and prevents the need for repeated procedures in the next 2-3 years. In view of the limited life expectancy of many dialysis patients with coronary artery disease, angioplasty may be preferred in some patients because of the lower rate of initial morbidity, and the possibility that the patient may be dead before subsequent revascularization procedures are required. It is clear that data on the outcome of medical therapy compared with angioplasty and bypass grafting in ESRD patients is necessary to enhance decision-making.

Reports on the efficacy of elective coronary stenting undertaken during cardiac catheterization compared with balloon angioplasty indicate that stenting decreases the need for repeated revascularization.

Cardiac arrhythmias: The following factors should be taken into consideration in the management of arrhythmias in dialysis patients.

1. Asymptomatic, non-sustained supraventricular arrhythmias and unifocal premature ventricular contractions that are not associated with symptoms and/or hemodynamic compromise usually do not require therapy.

2. Drug therapy of arrhythmias in dialysis patients is more complicated as compared with non-uremic patients because of possible alterations in pharmacokinetics, protein binding as well as additional drug clearance during dialysis. Also drug interactions should be kept in mind because dialysis patients are often on multiple medications. Many of the drugs used to treat arrhythmias may themselves become arrhythmogenic under certain conditions. The decision to treat arrhythmias with a specific drug should therefore be taken after carefully considering the risk benefit ratio and after consulting an experienced cardiologist.

Recently published pharmacokinetic data on anti arrhythmic drugs in renal failure are available and should be consulted[18].

3. Emergency treatment of symptomatic supraventricular tachy-arrhythmias include cardioversion and/or digoxin and verapamil for younger patients with good left ventricle function, followed by quinidine. Systemic anticoagulation is indicated in patients with chronic atrial fibrillation to decrease the risk of thromboembolic events.

Sustained ventricular tachycardia should be treated urgently with lidocaine followed by quinidine or mexiletine. Ventricular fibrillation should be managed with defibrillation followed by lidocaine.

Brady-arrhythmias may require permanent placement of a pacemaker in patients with syncope caused by sinus node dysfunction, sick sinus syndrome, high degree atrial ventricular block, and carotid sinus hypersensitivity.

4. Treatment of underlying cardiac disorders and correction of precipitable factors (electrolyte abnormalities) are of primary importance in the prevention of cardiac arrhythmias.

REFERENCES

1. Foley RN, Parfrey PS, Sarnak MJ: Clinical epidemiology of cardiovascular disease in chronic renal failure. *Am J Kidney Dis* 32 (Supl 3): S112-S119, 1998.
2. Sarnak MJ, Levey AS: Epidemiology of cardiac disease in dialysis patients. *Sem Dial* 12: 69-76, 1999.
3. Amann K, Ritz E: Cardiac disease in chronic uremia: pathophysiology. *Adv Renal Repl Ther* 4: 212-224, 1997.
4. Parfrey PS: Pathogenesis of cardiac disease in dialysis patients. *Sem Dial* 12: 62-68, 1999.
5. London GM, Guerin AP, Marchais SJ: Hemodynamic overload in end-stage renal disease patients. *Sem Dial* 12: 77-83, 1999.
6. Mitchell GF: Pulse pressure, arterial compliance and cardiovascular morbidity and mortality. *Curr Opin Nephrol Hypert* 8: 336-342, 1999
7. Foley RN, Parfrey PS: Anemia as a risk factor for cardiac disease in dialysis patients. *Sem Dial* 12: 84-86, 1999.
8. Prichard S: Dyslipidemia as a risk factor for cardiac disease in dialysis patients. *Sem Dial* 12: 87-90, 1999.
9. Rigatto C, Singal PK: Oxidative stress in uremia: impact on cardiac disease in dialysis patients. *Sem Dial* 12: 91-96, 1999.
10. Murphy SW, Foley RN: Divalent ion abnormalities and hyperparathyroidism in the etiology of cardiovascular disease of patients with chronic renal failure. *Sem Dial* 12: 97-102, 1999.
11. Bostom AG, Culleton B: Hyperhomocysteinemia in chronic renal disease: potential relevance to arteriosclerosis. *Sem Dial* 12: 103-111, 1999.
12. Lacson EK, Owen WF Jr: Interaction between hemodialysis adequacy and nutrition in dialysis patients. *Sem Dial* 12: 112-116, 1999.
13. Culleton BF, Wilson PWF: Thrombogenic risk factors for cardiovascular disease in dialysis patients. *Sem Dial* 12: 117-125, 1999.
14. Besarab A, Bolton WK, Browne JK, Egrie JC, Nissenson AR, Okamoto DM, Schwab SJ, Goodking DA: The effects of normal as compared with low hematocrit values in patients with cardiac disease who are receiving hemodialysis and epoietin. *New Engl J Med* 339: 584-590, 1998.
15. Foley RN, Parfrey PS, Morgan J y cols.: The effect of complete *vs* partial correction of anemia using erythropoietin on left ventricular structure in hemodialysis patients with asymptomatic cardiomyopathy. *J Am Soc Nephrol* (abstract); 9: 208A, 1998.
16. Locatelli F, Conte F, Marcelli D: The impact of hematocrit levels and erythropoietin treatment on overall and cardiovascular mortality and morbidity- the experience of the Lombardy Dialysis Registry. *Nephrol Dial Transplant* 13: 1642-1644, 1998.
17. Orth SR, Stöckmann A, Conradt C, Ritz E: Smoking as a risk factor for end-stage renal failure in men with primary renal disease. *Kidney Int* 54: 926-931, 1998.
18. Venkatesan J, Henrich WL: Cardiac disease in chronic uremia: management. *Adv Renal Replacement Ther* 4: 249-266, 1997.