Cardiovascular disorders are one of the most serious problems in chronic hemodialysis patients. According to the records of the last 15 years, 50% of these patients died from cardiovascular complications every year, without a marked reduction in the annual frequency of deaths. This gains even more importance when we consider the fact that, according to the Annual Report of USA Renal Data 1997, during the first year of treatment substitution a total reduction in the death rate from 30 to 24% has been achieved. This reduction is due to better follow-up and management of patients before their integration in programs of chronic renal dialysis.

The mortality due to cardiovascular disease in hemodialysis patients is estimated to be 9% annually and is 30 times higher than that observed in the general population. Even after correction for age, this percentage remains 10-20 fold higher than in the general population.

Consequently, there is a clear need for a systematic program of medical interventions in this area. These interventions concern two fields: I) the field of management of already known cardiovascular situations and events, and II) the field of reduction and modification of risk factors that lead to cardiovascular complications and adverse clinical events.

At this point, it is necessary to answer the question whether chronic hemodialysis patients – and patients with renal failure in general – have similar characteristics to those observed in the general population. Already it is known that acute pulmonary edema in this patient population is treatable only by hemodialysis, as the use of diuretics is not effective. Patients with renal disease constitute a unique population with particular epidemiological, clinical and therapeutic characteristics. This patient population should be studied systematically in order to determine the relevant vital therapeutic interventions for the improvement of patient outcome and prognosis.

Cardiovascular disorders in the hemodialysis population

During the last decade, a systematic effort has been made to determine the clinical profile, the epidemiology and the natural history of major cardiovascular diseases in patients with chronic renal failure who undergo hemodialysis, as well as the risk factors, and strategies for their prevention and management. However, only a small number of patients with renal failure have been included in epidemiological studies of cardiovascular disease or in long-term randomized clinical trials. The existing studies of cardiovascular disease in patients with renal failure are non-randomized trials or observations in non-representative samples. Consequently, a good deal of data concerning the main cardiovascular dis-
ese have not been clarified in the particular patient population.

However, epidemiological data show that both heart failure and coronary artery disease are expressed differently in hemodialysis patients than in the general population. A percentage of 30% of hemodialysis patients clinically have ischemic episodes with normal coronary angiograms, because of their particular characteristics, such as small vessel disease, coronary artery calcifications and left ventricular hypertrophy. Furthermore, cardiac dysfunction and failure may not be expressed only through peripheral edemas and dyspnea, but also through episodes of hypotension during hemodialysis.

According to expert opinion, the main cardiovascular disorders in hemodialysis patients are considered to be coronary artery disease (as in the general population) and left ventricular hypertrophy. Coronary artery disease is 4-8 times more frequent than in the general population. Left ventricular hypertrophy, because of high frequency and worsening prognosis, is considered to be not only a risk factor for de novo ischemic cardiomyopathy and de novo cardiac failure, but also a separate condition that directly increases the mortality of hemodialysis. Cardiac hypertrophy is 3 times more frequent in hemodialysis patients than in the general population.

Heart failure is 8 times more frequent in hemodialysis patients than in the general population and can be the result of coronary artery disease, left ventricular hypertrophy or other factors (e.g. anemia), or their combination. Many investigators have shown that cardiac dysfunction and failure are very powerful independent prognostic indicators of mortality in hemodialysis patients. Other independent prognostic indicators are coronary artery disease and left ventricular hypertrophy.

Management of hemodialysis patients: Patient subpopulations at risk and risk factors

The management of cardiovascular disease in patients with renal failure is based, as in the general population, on primary and secondary prevention. Primary prevention includes the modification of risk factors in patients at high and moderate risk for cardiovascular complications, as well as examinations aimed at the detection of coronary artery disease and left ventricular hypertrophy in low and moderate risk patients without a background or symptoms of cardiovascular disease. Secondary prevention concerns the management of patients with cardiovascular disease or patients with positive diagnostic tests for ischemia, who are classified as high or moderate risk groups.

The subpopulations of hemodialysis patients at risk are similar to those in the general population (Table 1).

In patients at low risk (without cardiovascular disease and diabetes mellitus, with one or no other risk factor) only modification of existent habits is recommended.

In patients at moderate risk (without cardiovascular disease but with many risk factors or with diabetes mellitus), interventions aim to reduce clinical events and risk factors through suitable pharmaceutical agents and changes in life style. Screening tests are also recommended for the potential detection of asymptomatic cardiovascular disease or in the case of some major non-cardiovascular surgical procedures.

However, most hemodialysis patients are classified into the high-risk group (with known history of cardiovascular disease and with more of one risk factors for coronary artery disease or with diabetes mellitus). Consequently, it is necessary not only to modify their life style but also to instigate proper pharmaceutical and/or interventional treatment.

The risk factors for cardiovascular disease in the particular patient population are divided into non-specific “classic” (which are similar to those of the general population) and specific (which exist only in hemodialysis patients).

Non-specific factors, as determined by the National Cholesterol Education Program in the USA, are classified into positive and negative.

Table 1. Groups of hemodialysis patients at risk for cardiovascular disease.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Patient group at risk</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Low</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>No</td>
</tr>
<tr>
<td>Risk factors</td>
<td>No</td>
</tr>
<tr>
<td>Aggressive</td>
<td>No</td>
</tr>
<tr>
<td>Medical</td>
<td>No</td>
</tr>
<tr>
<td>Changes of life style</td>
<td>Yes</td>
</tr>
</tbody>
</table>

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Positive risk factors:
Age: >45 years for men and >55 years or premature menopause without estrogen replacement treatment for women
Positive family history for acute myocardial infarction or sudden death at age <55 years
Smoking
Diabetes mellitus
Arterial hypertension: blood pressure >140/95 mmHg or administration of anti-hypertensive treatment
Decreased physical activity
HDL-cholesterol < 35 mg/dl in many measurements

Negative risk factors:
HDL-cholesterol > 60 mg/dl: A positive risk factor is removed when this negative factor exists.
The specific risk factors for hemodialysis patients are the following clinical entities:
- left ventricular hypertrophy
- hyperhydatosis
- hypoalbuminemia
- hypertriglyceridemia
- hyperlipoproteinemia (a)
- hyperhomocysteinemia
- anemia
- secondary hyperparathyroidism

Coronary artery disease in hemodialysis patients
The frequency of coronary artery disease in chronic renal failure patients without diabetes mellitus is ~20%. The respective percentage in diabetic patients is 30-50%, and this increases dramatically when the age is >45 years, especially in diabetics15,16. Eighty one percent of patients with diabetes mellitus have coronary artery disease13. The incidence of new clinical events increases by about 3% per year16. Silent ischemia has an incidence of ~75% in diabetic hemodialysis patients14. In non-diabetic patients, the respective percentage of silent ischemia has not been determined.

Important factors that promote atherosclerotic disease and lead to an increased incidence of coronary artery disease in particular population of patients are abnormal platelet function, pathological lipid and carbohydrate metabolism, reduction of endogenous fibrinolytic ability with a concomitant increase of pro-coagulant activity, increased oxidative stress, and endothelial dysfunction with impaired release of vasorelaxing factors (i.e. NO, prostacyclin)17.

The management of various common cardiological problems, such as angina, acute myocardial infarction, arrhythmias etc., is similar to that in the general population and will not be described further in this review. However, the importance of the regulation of extracellular volume and the correction of anemia for the management of hemodialysis patients with coronary artery disease should be stressed. We will proceed to a more extensive description of these factors, showing that without the correction of these abnormalities any special treatment is unlikely to be effective.

Generally:
- In the pharmaceutical field, medication is administered (nitrates, calcium antagonists, β-adrenergic blockers, etc.) as in the population of non-hemodialysis patients.
- Patients and their family are guided and encouraged to stop smoking, while they can also receive nicotine replacement therapy. In any case, recent smoking is considered as a risk factor. Thus, smoking cessation potentially leads to attenuation of its unfavorable effects and to the reduction of relevant risk to 50%18.
- Physical activity is also decreased in hemodialysis patients, so they should be encouraged to increase their activity with moderately intense exercise training (walking, cycling, jogging) of 30 min per day, 3-4 times per week, when this is feasible. At the same time, an increase in daily activities is recommended, such as gardening, domestic activities etc.
- There are no consistent data regarding the role of menopause and hormonal replacement treatment in women undergoing hemodialysis; therapeutic decisions must therefore be individualized5.
- There is insufficient clinical evidence regarding the effectiveness of aspirin administration in the population of hemodialysis patients. Additionally, in a recent study, aspirin has been associated with increased risk of thrombosis of arteriovenous grafts compared to dipyridamole19. However, because in the general population aspirin administration decreases ischemic episodes by 25% in patients with coronary artery disease and other cardiac disorders, 75-325 mg aspirin daily is considered reasonable in patients with chronic renal failure, when there no contraindications.

In hemodialysis patients with stable cardiovascular disease, enteric-coated tablets of aspirin are ad-
ministrated in usually low doses. Hemodialysis patients who undergo coronary angioplasty need higher daily doses of aspirin, e.g., 325 mg. Currently, aspirin is not used for the primary prevention of cardiovascular disease in hemodialysis patients, except in cases with very high risk, e.g., diabetics. In these patients, primary prevention with low doses of aspirin such as 75-160 mg daily is considered reasonable.  

Interventional procedures are preferred in high-risk patients, who remain symptomatic despite optimum pharmaceutical treatment. Hemodialysis patients have higher risk for adverse clinical events during aortocoronary bypass surgery, coronary angioplasty and coronary angiography.

Aortocoronary bypass surgery is preferred in hemodialysis patients, as it is a very effective procedure in terms of technical success and attenuation of symptoms. The operative mortality is about 8-9% in terms of technical success and attenuation of symptoms and varies between 0% and 20% in various reports. This percentage is three times higher than in the general population, and depends mainly on left ventricular function. It is considered that aortocoronary bypass surgery can improve survival in high-risk patients. Two-year survival varies between 45% and 92%, while the five-year survival is about 50%.

After coronary artery angioplasty, recurrence of symptoms associated with early restenosis is observed more often in patients with chronic renal failure (70%) compared to the general population (25-30%). An important factor limiting its effectiveness in this particular patient population is the high rate of vessel dissection during angioplasty. Coronary angioplasty with implantation of stents offers greater efficacy and is playing a gradually increasing role in the treatment of coronary artery disease in hemodialysis patients. More specifically, this technique has better results regarding the interventional treatment of one or more vessels with culprit lesions. Also, the use of rotablator atherectomy with simultaneous stent implantation appears to have satisfactory results in the therapeutic approach to coronary vessels with calcified lesions, decreasing the rate of restenosis and subsequent clinical events. Real revolution in the field of restenosis reduction in hemodialysis patients will bring in the near future the wide use of covered stents, vraschytherapy and the newer antiplatelet agents (IIb-IIIa inhibitors, clopidogrel, etc). However, despite the lower in-hospital mortality of coronary angioplasty compared to aortocoronary bypass surgery (5.1% vs. 14.2%), existing data suggest that coronary angioplasty is inferior to aortocoronary bypass surgery in terms of both the two- and five-year survival (51% vs. 66% and 18% vs. 70%, respectively). Finally, it should be noted that, with regard to the interventional management of coronary artery disease in hemodialysis patients, there are no randomized studies comparing the effectiveness of aortocoronary bypass surgery and coronary angioplasty with or without stents.

An important factor that is responsible for the creation of many major arrhythmiological problems (i.e., ventricular arrhythmias) in patients, particularly during the last hour of hemodialysis, is the presence of silent ischemia. The incidence of silent ischemia in this patient population is independent of age, sex, duration of hemodialysis, level of blood pressure and hematocrit, as well as the values of serum creatinine and sodium.

Regarding diagnostic tests for coronary artery disease, the majority of hemodialysis patients cannot undergo an ECG exercise stress test because of their exercise intolerance or because they are taking anti-ischemic medication. Thus, methods such as thallium or sestamibi scintigraphy and stress echocardiography are used, with concomitant administration of proper pharmaceutical substances (i.e., dipyridamole or dobutamine). The danger of triggering new ischemic episodes (i.e., angina, acute myocardial infarction) with these stress tests is low. Dipyridamole-thallium scintigraphy in these patients has sensitivity 37-86% and specificity ~75% while stress echocardiography with dobutamine has better respective percentages (69-95% and 95%) It should be pointed out that dynamic echocardiography with dobutamine appears to be superior to other dynamic tests with regard to the detection and evaluation of coronary artery disease in hemodialysis patients. Moreover, it can make an important contribution to the evaluation of hemodialysis patients with insulin-dependent diabetes mellitus before renal transplantation, estimating at the same time the size of cardiac cavities, the thickness of their walls and left ventricular systolic function. Hemodialysis patients who have positive diagnostic tests and are to undergo major surgical procedures should be evaluated with coronary arteriography.

Coronary artery disease diagnostic tests are not performed as routine examinations in asymptomatic hemodialysis patients (as in the general population). There are also no data to suggest that coronary revascularization would prolong survival in patients with silent ischemia. On the other hand, there is al-
ways the probability that these tests might cause new angina episodes or even acute myocardial infarction. Candidate recipients of renal graft who are at low risk for coronary artery disease also do not need to undergo these diagnostic tests (especially patients who do not have a history of coronary artery disease or congestive heart failure, and are non-diabetics and <50 years old).

Candidate recipients of renal graft who are at high risk for cardiovascular disease (i.e. patients who have history of coronary artery disease or congestive heart failure, as well as the diabetics who are <50 years and the non-diabetics >50 years old) must be examined in detail for the detection of active coronary artery disease. All candidate recipients of renal graft who are at very high risk (i.e. patients who have persistent myocardial ischemia or diabetes mellitus and are >50 years old) must proceed directly to coronary angiography.

Hypertension - Hyperhydatosis - Left ventricular hypertrophy

Arterial hypertension is an important risk factor for both coronary artery disease and left ventricular hypertrophy. Ninety-one percent of hemodialysis patients have arterial hypertension, while the respective percentage in the age- and gender-matched general population is 27%.

In the general population, high blood pressure (BP) is related with an increased risk of cardiovascular disease and high total mortality, while its regulation has been associated with decreased cardiovascular risk. In hemodialysis patients, an increased relative risk of death has been associated with high systolic BP >180 mmHg after the end of hemodialysis, as well as with low systolic BP < 130 mmHg (and mainly < 110 mmHg) before hemodialysis. On the other hand, there is a decreased relative risk in patients with systolic BP between 155-180 mmHg before the hemodialysis. As the arterial hypertension in hemodialysis patients is mainly volume-dependent, an important question that arises is what are the ideal quantities of water and salt that this particular patient population should receive?

In a long-term follow-up of these patients, it was found that an increase of BP by 10 mmHg or more dramatically increases the relative risk for death, left ventricular hypertrophy and dilatation, congestive heart failure and ischemic cardiomyopathy. On the other hand, hypotension reflects serious cardiac abnormalities and can mean myocardial dysfunction that is expressed clinically as congestive heart failure. Thus, arterial hypertension is a major risk factor for the development of chronic heart failure. Hypotension is also an important risk factor for death when congestive heart failure coexists.

According to the guidelines of the American Association of Hypertension, a BP < 120/80 mmHg is considered satisfactory. When patients receive anti-hypertensive medication, the treatment objective is the achievement of BP <140/90 mmHg.

The control of extracellular volume and the restriction of salt are of enormous importance, which seems to have been forgotten since the first decade after the application of hemodialysis. Unfortunately, certain misapprehensions related to dry body weight (DBW) are often observed. Thus:

- The DBW is not the usual weight after the hemodialysis course but the ideal weight, in which the regular volume state is achieved, without coincidental or asymptomatic hypotension but with a normal BP until the next course (without anti-hypertensive medication).
- DBW should not be confused and identified with the reduction of weight during the hemodialysis course. Thus, the BP levels in relation to weight reduction during the hemodialysis should not be investigated. It is unlikely that a correlation between them would be found, leading to the mistaken conclusion that BP is unrelated or is related very weakly to extracellular volume.
- Another important problem is the difficulty of estimating or achieving the DBW. Its clinical evaluation is not difficult, but requires time. It is based on the collection of simple data from the clinical history, on the estimation of peripheral edemas and the picture of jugular veins and, finally, on the cardiothoracic index in a chest X-ray. In cases of doubt, the method of “systematic step by step” progressive weight reduction (or increase) can be followed during certain weeks after the hemodialysis course, until normal and stable BP is achieved and maintained. This procedure presupposes the stopping of anti-hypertensive drugs, the cessation of short duration courses, and the use of solutions with low Na concentration (138 mM).

BP should be monitored with 24 hour BP Holter recordings, targeted at its regulation in the time intervals between hemodialysis courses. Anti-hypertensive drugs are not usually given during the day of hemodialysis, leading to loss of circadian rhythm and
to higher levels of mean BP for a longer time interval during the day. It has been also found that mean BP >99 mmHg is associated with dramatic increase of death rate\(^4\).

All categories of anti-hypertensive drugs, except diuretics, can be used according to the coexisting conditions\(^4\). Thus, calcium channel antagonists are used for the treatment of angina and left ventricular diastolic dysfunction, angiotensin converting enzyme (ACE) inhibitors for the treatment of congestive heart failure and, finally, β-adrenergic blockers for the attenuation of ischemic episodes or during the post-infarction period\(^5\).

On the other hand, it is necessary to carry out close monitoring of patients by echocardiography for the detection of potential left ventricular hypertrophy. The results of a large-scale French study are remarkable: although both ACE inhibitors and calcium channel antagonists achieved the same regulation of systolic and diastolic BP during one year, left ventricular mass detected by echocardiography decreased only with ACE inhibitors\(^4\).

Left ventricular hypertrophy, concentric or eccentric, is related, as an independent prognostic marker, with the increased mortality of hemodialysis patients\(^1\) as well as with de novo ischemic cardiomyopathy and cardiac failure\(^7,8,17\). The incidence of asymptomatic left ventricular hypertrophy in patients with renal failure varies between 50% and 75% and is positively correlated with BP levels and inversely correlated with hematocrit (Ht) values\(^8\). The existence of left ventricular hypertrophy is detected by ECG, chest X-ray (increased cardiothoracic index) and echocardiography. ECG abnormalities are more important than an increased cardiothoracic index, while the coexistence of the two findings means higher risk for cardiovascular complications\(^5\). The coexistence of ECG and echocardiographic findings implies a dramatic increase of cardiovascular risk\(^5\).

There is no evidence when the compensatory left ventricular hypertrophy becomes maladaptive. Echocardiographic findings associated with a higher risk of cardiovascular disease are an increased left ventricular mass and a decreased fraction shortening, increased left ventricular end-diastolic diameter, as well as the coexistence of left ventricular hypertrophy with increased end-diastolic diameter in women, and, finally, increased end-diastolic diameter and the combination of left ventricular dilatation with decreased fraction shortening in both genders\(^5\).

One important problem derived from left ventricular hypertrophy is hemodialysis hypotension, which appears in two forms: the hypotensive episodes at the end of the hemodialysis course which are observed in 15-50% of all hemodialysis courses, and the chronic hypotension observed in 5-10% of all hemodialysis patients\(^5\).

Several factors are responsible for hemodialysis hypotension\(^3\), such as the decreased plasma osmolality combined with an impaired peripheral vasoconstriction response, the high rate of hyperfiltration, the anti-hypertensive drugs, the reduction of adrenergic tone during the hypovolemic stress via the abnormal stimulation of the left ventricle and hypothalamus baroreceptors, the membrane’s biologic properties (via the cytokine activation which stimulates the release of prostaglandins and nitric oxide), the high temperature or the low sodium concentration of the hemodialysis solution, the consumption of a dinner before or during the hemodialysis course, and so on. Left ventricular hypertrophy facilitates diastolic dysfunction, reduction of stroke volume and finally, hypotension because of the abnormal adaptation of compensatory peripheral vasoconstriction responses\(^5\).

The management of left ventricular diastolic dysfunction is difficult, as a relatively small increase of volume can cause acute pulmonary edema. The administration of calcium channel antagonists that improve left ventricular relaxation can be a beneficial therapeutic intervention in those cases where BP levels permit their administration. Of the various methods proposed for the management of hemodialysis hypotension, the increase of sodium concentration (> 140 mM) in the hemodialysis solution, the reduction of solution temperature to 35 °C and the administration of a selective a1-adrenergic agonist such as midodrine may have the most beneficial effects\(^5\).

Hypercholesterolemia - Hypertriglyceridemia - Lipoprotein (a) - Homocysteine

Hyperlipidemia is observed in 45-50% of hemodialysis patients\(^5\). Increased values of total cholesterol >240 mg/dl have been reported only in 19% of patients, as in the general population. Moreover, a significant correlation between hyperlipidemia and cardiovascular disease has not been documented in this patient population. It has also been reported that low levels of cholesterol are associated with in-
creased cardiovascular mortality. However, similar findings have also been observed for body mass index and urea, indicating that low levels of cholesterol may be the result and not the cause of cardiovascular disease. Finally, a similar relation has been found between low BP and risk of cardiovascular death.

Low cholesterol levels have also been found in hemodialysis patients because of hyponutrition. Hyponutrition is observed in 25% of patients, and a decline of cholesterol by 25 mg/dl leads to 10-fold higher mortality. Thus, an ostensibly higher risk of death is created. The real risk of death increases when the values of cholesterol are increased (relative risk ~3 for cholesterol 300 mg/dl versus 100 mg/dl). Consequently, the perception that a high cholesterol level is not harmful for hemodialysis patients is not only wrong but also dangerous, since high cholesterol values increase the risk of cardiovascular complications. Table 2 summarizes lipid values found in hemodialysis patients and in the general population.

Hemodialysis patients with cardiovascular disease exhibited higher levels of triglycerides, VLDL-cholesterol, total cholesterol, LDL-cholesterol and lower levels of HDL-cholesterol than those without cardiovascular disorders. Patients who die from cardiovascular complications have higher levels of triglycerides. In diabetic hemodialysis patients, cardiovascular complications and cardiac death are associated with low HDL-cholesterol values. It has also been found that hemodialysis patients with a rapid increase in the total amount of coronary artery calcification have higher triglyceride levels and lower HDL-cholesterol levels compared with patients who exhibit slow progress of coronary vessel lesions.

The values of total cholesterol should be <200 mg/dl, even if in most reports the limit is 240 mg/dl. Therapeutic target is LDL-cholesterol <100 mg/dl, HDL-cholesterol >35 mg/dl, and triglycerides <200 mg/dl. Criteria of treatment are the existence of risk factors, and the values of LDL- and HDL-cholesterol. Therapeutic decisions are taken on the basis of LDL-cholesterol values.

Diet is recommended when LDL-cholesterol is ≥100 mg/dl, while medication is administered when LDL-cholesterol is ≥130 mg/dl. The most effective drugs without significant adverse effects (first choice) are statins, which can be combined with niasin or fibrates when triglyceride values are high. Values of triglycerides should also be evaluated: statins or re-
Scientific data regarding the relation between homocysteine levels and cardiovascular disease are limited. A positive correlation between them has been found only in male patients. In another study, it was found that in patients with homocysteine values in the upper quartile, the incidence of cardiovascular disease was 45%, while in those with values in the lower quartile the respective incidence was 29%. The same study also reported that the relative risk of cardiovascular complications or death increases by 1% for each 1mM of homocysteine concentration increase, with possible mechanisms the vascular endothelium damage, the activation of pro-inflammatory cytokine cascade and the increased oxidative stress.

High doses of folic acid are given: 15 mg/24 h in addition to 1-2 mg/24 h that are normally administered, thus leading to a reduction of homocysteine levels by 25-30%. Furthermore, treatment with N-acetylcysteine is also effective.

In any case, there is no established treatment, nor do sufficient data exist to indicate that a dramatic reduction of homocysteine levels also decreases the risk of cardiovascular events in hemodialysis patients.

Hypoalbuminemia

The most constant parameter associated with the increased mortality of hemodialysis patients is low serum albumin levels, reflecting either hyponutrition or inflammation. A potential correlation between hypoalbuminemia and progression of left ventricular concentric hypertrophy or dilatation has not been found. In contrast, a very powerful correlation of hypoalbuminemia with recent beginning of ischemic cardiomyopathy or cardiac failure and death has been observed. Hypoalbuminemia potentially exerts its deleterious effects by promoting the development of cardiomyopathy, although the relevant pathophysiological mechanisms have not been yet clarified.

Parathyroid hormone - Anemia - Hemodialysis efficiency

During the last years, important scientific progress has been made in the management of uremia, secondary hyperparathyroidism and anemia in hemodialysis patients. This progress is due to the rapid development of technology, improvement of clinical experience in hemodialysis, use of vitamin D and administration of human recombinant erythropoietin. However, regarding these fields only a few relevant data will be reported in this cardiological review.

Elevated parathyroid hormone levels and anemia are considered to increase the risk of left ventricular dysfunction and hypertrophy.

Anemia is closely related with progressive left ventricular dilatation and systolic dysfunction, congestive heart failure and increased mortality (due to cardiomyopathy and cardiac failure). Left ventricular mass was found to reduce by 26% and hemoglobin (Hb) to increase in parallel from 8 to 10.8 g/dl after administration of erythropoietin for 6-9 months in hemodialysis patients, although there was not a respective control group. It has also been observed that, in a range of Ht levels between 16% and 36%, Ht decrease by 1% is accompanied by an increase in mortality of 12.5%, after the proper adjustment for age, Kt/V ratio (a marker of hemodialysis efficiency) and protein catabolism rate. The risk of cardiovascular death is increased when Ht levels are <30% and >35%.

Ht / Hb ratio values, as an ideal therapeutic target, have not still been determined.

Secondary hyperparathyroidism is among those disorders that predispose to rapid calcification progression into the cardiac valves and coronary arteries of hemodialysis patients. Ten to 50% of hemodialysis patients have mitral calcifications and a 25-55% have aortic valve calcifications. The percentage of hemodialysis patients with coronary calcifications has also been found to be 10-fold higher compared to age-matched healthy controls, using computed beam tomography. These findings are associated with increased values of calcium x phosphorus product because of hyperphosphatemia and/or hypercalcemia, as a result of metabolism disturbances of these ions in renal failure, of treatment with vitamin D, and of increased Ca reception via phosphorus-binding agents contained Ca or hemodialysis solution. Additionally, a score of coronary vessel calcifications has been proposed, aiming at risk stratification for coronary artery disease. A high coronary calcification score has been correlated with increased incidence of acute myocardial infarction and angina. On the other hand, a high score for aorta calcifications has been associated with increased incidence of intermittent claudication.

Uremia itself and non-biocompatible materials of hemodialysis are also responsible for the pathogenesis of cardiovascular disease, promoting the ath-
erosclerotic process through an increase in oxidative stress and the production of pro-inflammatory and chemotactic cytokines. A higher rate of deaths has also been associated with a low Kt/V in hemodialysis patients.

Insufficient hemodialysis, with concomitant hypohydration and anemia, are the major parameters associated with the development of hemodialysis pericarditis, which is observed in 13% of chronic hemodialysis patients.

Hemodialysis pericarditis is manifested via chest pain, which characteristically is intensified in the supine position, fever, pericardial friction and pericardial effusion identified by echocardiography in at least 50% of cases, or cardiac tamponade. Formal elevation of ST interval and consequent T wave changes may not always exist, potentially because epicardial damage is infrequent.

This complication is treated with intensive hemodialysis (without heparin in order to avoid the increase of bleeding in pericardial cavity), taking care to maintain BP within normal limits and to avoid hypocalemia and/or hypophosphatemia. Non-steroids, anti-inflammatory drugs and corticoids are used when intensive purgation does not have results, because these agents do not accelerate the attenuation of pericardial inflammation/liquid collection and potentially have side effects.

When pericardial liquid increases or is not improved during a two-week time interval, as well as in moderate fluid collections >250 ml, an intervention- al removal of pericardial liquid is applied. Pericardiectomy is recommended, under local anesthesia, with or without placement of an endopericardial catheter for fluid removal, with good results and relatively few complications. Pericardiectomy, under general anesthesia, is necessary only after the failure of pericardiectomy, because of the increased mortality involved. Emergency pericardiocentesis should be used only for cardiac tamponade with shock, because this procedure also has a high mortality.

Diabetes mellitus

Diabetes mellitus is found in 33% of patients with renal failure, and this patient population is affected by coronary artery disease in a percentage of ~80%, with a high incidence of premature death from cardiovascular complications. In hemodialysis candidate recipients of renal graft, coronary arteriography showed in 50% of them one or more stenoses >50%, and 30% of these stenoses were >75%. This relation also depends on age: stenoses >50% have been found in diabetic hemodialysis patients > 45 years.

Hyperglycemia causes damage of the vascular endothelium with a variety of mechanisms contributing to the creation of atherosclerotic disease, and also has a direct atherogenic action. In the general population, a strict control of blood glucose is necessary, with reduction of blood glucose concentrations to within normal limits: pre-prandial glucose=80-120 mg/dl, nocturnal glucose =100-140 mg/dl and glycosylated hemoglobin (A1cHb) levels < 7%. A strategic target of these restrictions is the reduction of diabetes mellitus complications.

However, in the population of diabetic hemodialysis patients, the respective relation of hyperglycemia degree with cardiovascular complications has not been determined. Many data suggest that the strict control of glycemia is not necessary, because diabetes pre-exists for many years and has already caused its complications. On the other hand, there is always the danger and consequences of hypoglycemia with the strict regulation of blood glucose. It must be also noted that A1cHb levels are falsely lower in badly treated diabetes in hemodialysis patients because of the decreased survival time of red blood cells. For this reason, mean values of pre-prandial glucose and nocturnal glucose should be evaluated. On the other hand, decisions regarding the strict regulation of blood glucose should be individualized. As there is no need for a strict control of diabetes, target values for A1cHb should be ~8% and for pre-prandial glucose ~100-150 mg/dl. This control achieves protection of hemodialysis patient from metabolic and infectious complications of hyperglycemia with a low danger of hypoglycemia.

References

Cardiovascular Diseases in Hemodialysis Patients


