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HEART COMPLICATIONS OF KIDNEY FAILURE

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ABSTRACT: Through many general and specific risk factors, renal failure is involved in the development of cardiovascular complications, increasing cardiovascular morbidity and mortality in this type of patients. Early diagnosis of these complications is necessary in any patient with renal failure. Echocardiography is a key element in predicting cardiovascular events. The treatment mainly involves the treatment of general risk factors but also specific risk factors and requires cooperation between the cardiologist and the nephrologist.

Keywords: Renal failure, cardiovascular disease, specific risk factors, Uremic cardiomyopathy.

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1.INTRODUCTION

With increasing prevalence and incidence, high cost of care and widespread leading causes (diabetes and high blood pressure), chronic end-stage renal failure is a major public health problem in both developed and emerging countries. [1] Chronic renal failure is defined as: renal impairment (histological, abnormal urinary sedimentation, pathological imaging) or glomerular filtration rate (GFR) <60 ml / min / 1.73 m² for at least three months. [2] Calculation of the glomerular filtration rate by measuring the clearance of an exogenous substance such as inulin or isotopic tracers (51Cr-EDTA, iohexol, 125I-iothalamate) is the most accurate way to estimate renal function. However, these techniques are difficult to perform in clinical practice and are reserved for study protocols or difficult cases. An endogenous substance, creatinine, is used to estimate glomerular filtration rate using equations that take into account age, sex, race, and weight. These two equations are:

1. The Cockroft-Gault equation: (140 - age) x weight [kg] x 1.03 [for women] and 1.23 [for men].
2. Simplified equation from the MDRD study: 186.3 x creatinine - 1.1547 [mg/dl] x age - 0.203 x 0.742 [for women] and 1.21 [for African-Americans].

There is a strong association between chronic renal failure and cardiovascular disease, the more the GFR decreases the higher the risk of cardiovascular disease increases. Cardiovascular complications are the leading cause of morbidity and mortality in patients with chronic renal failure who are on dialysis or in the pre-dialysis stage. [3] Cardiovascular mortality is three to twenty times higher in dialysis patients than the general population of the same age. A high prevalence of cardiovascular morbidity is present from the beginning of the substitute treatment and is predictive of mortality in dialysis. [4,29] The initial publication of the Scribner group in 1974, highlighted the abnormally high incidence of cardiovascular death in hemodialysis patients [5], 61% died from cardiovascular disease: myocardial infarction, heart failure, stroke. In a study conducted by Go and al. with more than one million patients with chronic renal failure, annual mortality and cardiovascular morbidity were 11.4% and 21.8%, respectively, in stage 4 patients. [6] Keith et al. found that 46% of a cohort followed for 5.5 years died from cardiovascular disease before dialysis. [7] Post-mortem anatomical studies showed a significantly higher prevalence of carotid or ilio-femoral atheroma in dialysis patients than in subjects of the same age in the general population. [8]

2. MATERIALS AND METHODS

In this research, we did a review of the literature. In fact, we collected 101 articles concerning cardiac pathology during renal failure. We looked for all the general and specific factors involved and we detailed the cardiac complications secondary to kidney failure. We also discussed the value of transthoracic echocardiography for screening and diagnosis of these complications.

3. RESULTS AND DISCUSSION

Few data exist in Morocco on concerning the epidemiology of chronic end-stage renal failure, its incidence, modeled on the Maghreb countries, is estimated between 100 and 150 new cases/ 10^6 people / year (or ≈ 3000- 4500 new cases / year), its prevalence has 167 cases / 10^6 people. It should be noted that 80% of chronic end-stage renal failure is not managed on dialysis. [9] The national registry for data on chronic end-stage renal disease, MAGREDIAL (Morocco dialysis transplant), which is currently functional, represents a health policy adapted to this public health problem. In the United States, the USRDS (United States Renal Data System) statistics found a mortality rate of 23.1% per year in dialysis patients, of which 52% were cardiovascular (Myocardial infarction 10,7%, heart failure 15.9%, cardiac arrest or sudden death 19.8%, stroke 5.8%). [10] In Canada, in a cohort of 433 dialysis patients, 58% of deaths were cardiovascular (10.1% myocardial infarction, 11.4% heart failure, 25.5% sudden death, 10.7% peripheral arterial disease). [11]

Pathophysiology:

Classical risk factors do not fully explain this increased risk of cardiovascular disease, which appears to be influenced by specific risk factors for kidney failure. [3]

Classical risk factors:

- **Age and male sex:**

The adverse influence of age and sex is well established in the general population. It is expressed in the same way in uremic patients, but with a much higher incidence of cardiovascular complications at equal age. [4]

- **High blood pressure:**

High blood pressure is a major factor in cardiovascular morbidity and mortality. In the study by Foley and al. each 10 mmHg increase in mean arterial blood pressure in dialysis patients was associated with a 48% increase in the risk of developing left ventricular hypertrophy (LVH) and developing heart failure. [13] In the Levin and al. study, each 5 mmHg increase in systolic pressure was associated with an 11% increase in the risk of LVH. [14] High blood pressure promotes, by itself, the development of atherosclerosis due to the alteration of the endothelium resulting from tension constraints and the oxidative stress it causes. [15] High blood pressure and atheroma exert reciprocal deleterious effects. Atheromatous stenosis of the renal arteries can create, or increase, hypertension. Moreover, by depriving the ischemic kidneys of self-regulation of soda excretion by atrial natriuretic factor, it promotes the occurrence of repeated episodes of pulmonary oedema. [16]

- **Smoking:**

Smoking is a major factor of atheroma in the general population [17] and uremic patients. Nicotine increases the oxidative stress and peroxidation of lipoproteins. The effects of smoking are amplified in uremic patients because of the retention of nicotine resulting from the reduction of renal function. [18]

- **Diabetes:**

In the Foley and al. study, the risk of cardiovascular mortality in dialysis was twice as high in diabetics as in non-diabetics, mainly because of an increased risk of coronary artery disease and ischemic heart disease. [19] In the study done by Koch and al. involving 412 diabetic patients on dialysis in 25 centers in Germany, cardiovascular events accounted for 61% of the observed causes of death. [20]

- **Dyslipidemia:**

Secondary dyslipidemia in the uremic patients is particularly atherogenic, especially since it is present in the early stage of chronic kidney disease. It combines a decrease in HDL cholesterol, an increase in LDL cholesterol and triglycerides, a decrease in apolipoproteins AI and AII and an increase in apolipoprotein B. [21] Elevation of lipoprotein (a) (Lp (a)), very atherogenic, is common in uremic patients and increases the risk of atherosclerosis. [22] There is also a disproportionate

increase in apoCIII concentration compared to apoCII [23], with a correlation between apoCIII elevation and atheromatous hemodialysis patients. [24] The atherogenic effect of dyslipidemia is further increased in uremic by LDL peroxidation. [25]

- **Hyperfibrinemia:**

Hyperfibrinemia has been identified as a major and independent risk factor for atheroma in the general population. It is almost constant in the uremic patients [22]. In a cohort of non-dialyzed chronic kidney disease, fibrinemia was higher, on average, in uremic patients than in controls and, among uremic patients, higher in patients with myocardial or cerebral infarction than in those who remained free from these complications. [26]

- **Hyperhomocysteinemia:**

Hyperhomocysteinemia is also an independent risk factor for atheroma in the general population, as in uremic dialysis [27] and predialysis. [26] In patients with renal failure, hyperhomocysteinemia is constant and proportional to the degree of chronic kidney disease (CKD). In the advanced stages of CKD and dialysis, the plasma concentration of total homocysteine can be three to four times the average value seen in normal renal function subjects. Hyperhomocysteinemia is further increased by a deficiency of folate, pyridoxine and / or vitamin B12, common in uremic patients. [27]

Specific risk factors for renal failure:

- **Volume and barometric overload:**

Koell and al. have detected in a large cohort that fluid overload is associated with a higher hospitalization rate for cardiovascular reasons and / or death. [28] Pressure and volume overload induce left ventricular hypertrophy and in the absence of interventions that reduce left ventricular overload, the adaptation is triggered, leading to increased cell death and fibrosis myocardial. As a result, there is a decrease in capillary density, diastolic dysfunction, intraventricular conduction disorders, left ventricular dilatation. [29]

- **Arteriosclerosis:**

The work of G. London's group has clearly demonstrated the role of remodeling of large-caliber elastic arteries (aorta, carotids). This process is characterized by the dilatation, thickening and induration of the wall of these arteries. [30] These changes are developed in response to the same pressure and volume constraints that lead to remodeling of left ventricle. The resulting arterial rigidity increases systolic pressure and pulsating pressure, thus aggravating LVH. [15]

- **Anemia:**

Anemia has been recognized as a major and independent factor of LVH. In the retrospective study of Madore and al. the mortality rate was twice as high in hemodialysis patients with hemoglobin levels lower than 8 g/dL compared to patients with hemoglobin between 10 and 11 g/dL. [31] In pre-dialytic CKD, A. Levin's studies showed a correlation between the degree of anemia (itself proportional to the degree of renal failure) and the presence of LVH demonstrated by

echocardiography [32]. Each 0.5 g/dL decrease in hemoglobin was associated with an increased risk of LVH of 32%. [14]

In the Canadian prospective study, each decrease in hemoglobin of 1 g/dL was associated with an increased risk of LVH of 46%. [33] Anemia also increases the consequences of coronary atheroma and myocardial ischemia.

- **Phosphocalcic disorders and secondary hyperparathyroidism:**

The alteration of phosphocalcic metabolism occurs by promoting the formation of calcium deposits in the media of the arteries, including coronaries. [34] They cause valvular and arterial calcification and occlusion of the coronary, cerebral and peripheral arteries. Hyperphosphoremia has been found to be associated with the risk of cardiovascular death in hemodialysis patients [35]. Patients with a phosphorus greater than 65 mg / l (≈ 2 mmol / l) or a high phosphocalcic product had a mortality of 30% higher than patients with controlled phosphoremia. [35]

- **Arteriovenous fistula:**

Responsible for an overload of volume. Indeed, high-rate arteriovenous fistulas increase cardiac output and may lead to heart failure. This complication can be easily prevented by monitoring the fistula flow using Doppler ultrasound, and by surgical reduction of the flow if necessary. [36]

- **Uremic toxins:** leading to myocardial fibrosis.
- **Hypoalbuminemia:**

Hypoalbuminemia has been identified as the most significant predictor of mortality in dialysis patients [37], suggesting that caloric-protein malnutrition plays a role in the excess mortality observed in dialysis uremic patients. [38,39] However, malnutrition is rarely reported as a direct cause of death in dialysis patients [48] and cachexia is reported in only 2.5% of cases in the USRDS registry. [41] Malnutrition is not the only cause of hypoalbuminemia. The decrease in hepatic synthesis of albumin is part of the acute phase reaction, in contrast to CRP and fibrinogen, whose hepatic synthesis is increased during the inflammatory reaction. [42,43]

- **The renin-angiotensin system:**

Appears to play a proper role of the functional alteration of left ventricle, as evidenced by the fact that angiotensin converting enzyme inhibitors cause a partial regression of the LVH regardless of their antihypertensive effect. [44]

- **Oxidative stress:**

The role of oxidative stress and inflammation in atherosclerosis of the uremic patients has been highlighted [45,46,47]. In the early stage of CKD, there is a chronic inflammatory resulting from the activation of monocytes, lymphocytes and polynuclear cells. This results in excessive production of pro-inflammatory cytokines and oxidants, [48,49], which contributes to endothelial cell damage, an initial step in atherogenesis. [50]

- **Race:**

The prevalence of cardiovascular morbidity at the beginning of dialysis is higher in caucasian patients than in black patients, which may explain, in part, the better survival of dialysis patients. [51]

- **Vasoconstrictor factors:**

Alterations in the balance of vasoconstrictor and vasodilator factors, and pro- and antithrombogenic factors have been described in uremic patients. The plasma concentration of endothelin-1, a potent vasoconstrictor, is increased in dialysis patients and non-dialysed patients, as well as noradrenaline [52]. The synthesis of nitric oxide (NO), a potent vasodilator, is inhibited in uremic patients due to the accumulation of the competitive inhibitor of NO-synthetase, asymmetric dimethyl-L-arginine (ADMA) [53] and the concentration of ADMA was found to be 2-fold higher in hemodialysis patients with atherosclerotic manifestations than in those free of these complications. [54]

Complications:

Uremic cardiomyopathy:

The mechanisms of uremic cardiomyopathy are multifactorial and their effects are cumulative. LVH is, by itself, a major predictor of death from heart failure in both general population and uremic dialysis. [13,55] The rarefaction of capillaries, myocardial fibrosis and the destruction of myocytes contribute to myocardial ischemia and functional impairment of the left ventricle. [56] Evidences indicate that progression of LVH in individuals with CKD is predictive of cardiovascular events, independent of baseline values of left ventricle mass. A weight gain of 1 g/ m to the power of 2.7/month was associated with a 62% increase in the risk of a fatal and non-fatal cardiovascular event [57]. This suggests that changes in the left ventricle mass index represent a stronger predictor of cardiovascular mortality and complications than the left ventricle mass itself, and periodic echocardiographic studies may be useful in clinical practice. The development of accelerated atherosclerosis, in the uremic, is due to the intervention of classical and specific risk factors of renal insufficiency whose effects are additive. [4,15,58] Diastolic dysfunction has been reported as an independent predictor of mortality. [59,60]. It can develop early in CKD [61] and is common in later stages. For example, in a small study in kidney transplant patients, 67% had diastolic dysfunction [62]. Although left ventricular mass decreased by 23% after transplantation, diastolic dysfunction persisted in most cases, indicating irreversibility of structural changes, probably due to long-term fluid retention and myocardial fibrosis. Several studies have suggested that uremic cardiomyopathy first begins with diastolic dysfunction, which then develops into progressive fibrosis and ventricular hypertrophy. Aggressive intervention at an early stage may prevent irreversible cardiac remodeling and the associated poor prognosis. [63,64] While NT-proBNP is a clinically valuable biomarker in the diagnosis of heart failure in the general population, it is elevated in patients with CKD due to

decreased renal excretion [65]. The use of NT-proBNP alone in screening for diastolic dysfunction in patients with CKD is limited suggesting the need for additional cardiac imaging. [66]

Valvular heart diseases:

Valvular heart diseases are an additional factor of heart failure, including calcified aortic stenosis, which has the characteristic of being able to worsen abruptly and whose reconstructive surgery is burdened with a heavy mortality.

Conduction Disorders:

The increase in electrical excitability is related to a higher incidence of sudden death in this group of patients. [67]

Rhythmic disorders:

Favored by ionic disorders (especially potassium). The size of the left atrium has been shown to be independently associated with cardiovascular mortality [68]. In addition, left atrial dilatation favors atrial fibrillation, a known risk factor for cardiovascular events in renal failure [69,70] and, consequently, arterial thromboembolic complications.

Pericarditis:

The pericarditis of chronic renal failure hemodialysis is the consequence of several factors including a deficient vascular approach and an insufficient dialysis dose. The installation of uremic pericarditis is often insidious, hence the need to systematically look for it in chronic hemodialysis patients.

Treatment:

Interest of early treatment:

Cardioprotective treatment must become an essential component of the treatment of patients with chronic renal failure, as well as nephroprotective treatment. It combines the optimal treatment of the classic risk factors as well as the specific factors of the CKD. The preventive efficacy of this treatment depends on the precocity of its implementation as early as the pre-dialysis period. Many studies have shown that late nephrology management of CKD is associated with higher morbidity. [71,72] A retrospective study of all 1152 uremic patients who started dialysis at Necker Hospital between 1989 and 1998 [73] showed that patients who received regular nephrology follow-up at least three years before the start dialysis patients had a prevalence of cardiovascular morbidity that was half that of patients under 6 months of age. In addition, this study showed that the long-term mortality rate for dialysis was twice as low in patients who received prialytic follow-up for at least three years as in those given to the nephrologist at a later stage.

Left ventricular hypertrophy:

Left ventricular hypertrophy is a major target for intervention during CKD. An interesting study showed that improvement in mass index and systolic function over a period of one year after initiation of dialysis treatment was associated with a decrease in the probability of heart failure, but not ischemic heart disease. [74] The prevention of LVH first passes through the control of

hypertension [75]. The optimal target level of blood pressure to be reached has been defined by <130/85 mmHg in the absence of proteinuria and <125/75 if proteinuria exceeds 1 g / day. The molecules inhibiting the effects of angiotensin II, are preferred because of their anti-proteinuric action and their favorable cardiovascular effects, especially in patients with diabetic nephropathy. [76] Their use should be cautious and well monitored in elderly and / or atheromatous patients, at risk for renal artery stenosis. Combination therapy is most often required to achieve optimal blood pressure control, combining angiotensin II inhibitors, diuretic of the handle, calcium channel blockers and beta-blockers. [75]

Volume overload:

In dialysis patients, well-controlled ultrafiltration, adjustment of natremia, maintenance of optimal dry weight and appropriate salt and water intake help to control high blood pressure and avoid tension drops in dialysis. Treatments to correct fluid overload can reduce the risk of developing diastolic dysfunction and improve cardiovascular outcomes in patients with CKD. The interdialytic weight gain should be as small as possible, especially in the elderly, with low arterial compliance. [44,77] Regular monitoring of fluid status by bioimpendence spectroscopy (BIS) and NT-proBNP can be used to find a patient at risk of developing diastolic dysfunction. [78]

Anemia:

Appropriate supplementation with iron (intravenous in hemodialysis, oral most often in non-dialyzed CKD) must be ensured, as well as supplementation with folic acid and vitamins B6 and B12. Recombinant erythropoietin has transformed the quality of life of uremic patients, dialysis and non-dialysis patients.

Dyslipidemia:

It seems reasonable to adopt in uremic patients the recommendations used in the general population [79] for the implementation of lipid-lowering treatment, considering uremic patients as belonging to the highest risk group. Lipid-lowering therapy is considered justified as soon as LDL-cholesterol exceeds 3.4 mmol / l (130 mg/dl). The treatment is more indicated if the patient is diabetic or already has atheromatous cardiovascular disease. The first stage of treatment is based on reducing saturated fat and fast absorption sugars. The reduction of animal protein helps to limit the saturated fats. However, the reduction of lipids and fast-absorbing carbohydrates is limited by the need to avoid a calorie deficit [79]. The help of a dietician is invaluable to guide the diet in a favorable way. [80]

In hemodialysis patients, the use of high permeability membranes with high convective transfer and apolyproprotein adsorption properties would improve the lipid profile. [81] Fibrates (particularly Gemfibrozil) are most indicated for hypertriglyceridemia, while statins are more appropriate for elevated LDL cholesterol [82,83]. The use of fibrates or statins imposes a close monitoring of creatinine phosphokinase (CPK), in order to detect possible muscle damage and prevent the occurrence of rhabdomyolysis. Indeed, most fibrates are eliminated by the kidney and renal failure

can cause accumulation, while the pharmacokinetics of statins is, in principle, not changed [84]. However, it is advisable to start the treatment at half dose, and increase it cautiously by controlling the CPK rate. [83,84]

Smoking :

A special effort should be made with uremic patients to explain the deleterious effects of smoking and encourage them to wean.

Sedentarity :

The maintenance of a physical activity adapted to the possibilities of the patient, for example walking 30 minutes a day, is recommended.

Hyperhomocysteinemia :

The folic acid intake significantly reduces the plasma concentration of homocysteine. In the pre-dialysis stage, an oral dose of 5 mg three times a week is sufficient, this intake being raised to 5 mg / day in case of treatment with erythropoietin [85]. In hemodialysis, a daily dose of 5 mg orally is usually sufficient, but the intravenous route is more effective. In all cases, supplementation with vitamins B6 (piridoxine), at a rate of 250 to 500 mg / week is indicated, combined with vitamin B12 supplementation (1 mg per week orally).

Diabetes : Strict glycemic control is imperative in diabetic uremic patients.

Thrombogenic factors :

Low dose of antiagregant aspirin (75 to 100 mg / day) reduces the risk of thrombosis, of atheromatous vessels in the general population [86] and appears recommended for primary and secondary prevention. [87]

Oxidative stress and inflammation :

To date, no measure has been proven to be effective in preventing oxidative stress in uremic patients. The effect of vitamin E supplementation is discussed. In hemodialysis, the use of biocompatible membranes makes it possible to reduce the oxidative stress and the release of pro-inflammatory cytokines generated during each hemodialysis session.

Secondary hyperpathyroidism :

Its prevention is a major component of uremic treatment, both dialyzed and pre-dialyzed. Sufficient, but not excessive, calcium supplementation and the prevention of hyperphosphoremia are critical to avoid the cardiac and arterial consequences of a marked increase in phosphocalcium product. Calcium channel blockers have the property of limiting the increase in intracellular calcium and also help to limit the risk of cardiovascular events. [88]

Dyskalemia : Dyskalemia should be avoided because it increases the risk of rythm disorders.

Diet : The Mediterranean diet rich in mono-unsaturated lipids resistant to oxidation and the consumption of fish rich in polyunsaturated lipids, as well as the moderate consumption of red wine, rich in antioxidant flavonoids, may be recommended to uremic patients. [89]

Interest of the ETT :

In dialysis patients, the value of echocardiography for predicting cardiovascular events and mortality has been reported. [55,90] Mass echocardiography mass monitoring is an interesting additional clinical tool in assessing the prognosis and success of interventions which lead to LVH regression. [74] Echocardiography allows evaluation of ventricular mass and volume, and has excellent accuracy for detecting hypertrophy, defining its geometric pattern (concentric or eccentric), and quantifying systolic function. In addition, Doppler-derived techniques can generate information about ventricular relaxation and its filling dynamics, as well as the presence of abnormalities in the heart valves and pericardium. In a Canadian study of a cohort of 432 dialysis patients, only 16% had a normal echocardiogram. The increase in E-speed is mainly related to sodium and water retention, while the decrease in TDI-measured speed represents an increase in ventricular stiffness. In patients undergoing hemodialysis, the speed E is high before the dialysis session and then decreases after ultrafiltration because of the decrease in circulating volume [91]. On the other hand, E' remains similar after ultrafiltration. In other words, E', which measures the mitral annular diastolic velocity, is relatively unaffected by the volume status of the patient. [92] A recent Australian study followed a cohort of 129 patients with end-stage CKD (without evidence of LV ischemia on echo-stress) for more than 2 years, demonstrating that E' added an independent prognostic value to clinical parameters [93]. The ratio of early diastolic velocity of E and E' mitral flow (E / E') was the best non-invasive predictor of high LV filling pressure. [94] Another form of assessment of diastolic function is measurement of left atrial volume. Unlike Doppler indices, which provide us with momentary and transient information about LV filling, left atrial volume acts as a chronic marker of diastolic function, reflecting the long-term effect of increasing filling pressures. A person undergoing hemodialysis is subject to significant variations in body weight, whether it is an alteration of the blood volume or a compromised nutritional status, which may lead to an erroneous assessment by indexing the surface body. A proposed indexation based on height at power of 2.7 [95] appears to be the most accurate estimate of LV mass in this group of patients. It is important to recognize that some of the alteration of LV geometry in patients with CKD may be related to the time the echocardiogram was performed. Shortly after the dialysis session, it is common to see a reduction in the diastolic diameter of the LV and an increase in the thickness of the LV wall as a pure consequence of the volume depletion by ultrafiltration. Similarly, the examination performed shortly before the start of the session may present a diagnosis of LV enlargement with eccentric hypertrophy which will be "converted" into concentric at the end of the session. Such fluctuation may lead to an incorrect assessment that could be minimized by performing the echocardiogram during the interdialytic period. [96]

The rise of troponin during renal failure:

In patients with renal failure, there are many false positives and a poor positive predictive value.

There is an elevation of troponin T in about 53% of patients with CKD, compared to 7% for troponin I [99]. With an ultrasensitive method, troponin T is detectable in 81% of these patients, and this value is inversely proportional to the decrease in glomerular filtration rate. The reduction of GFR as the unique cause of this phenomenon remains debated. In contrast, comorbidities (hypertension, ventricular hypertrophy, diabetes) increase the probability of high rate of troponin. Uremia, activation of the renin-angiotensin system, oxidative stress and phosphocalcic disturbance further contribute to the progression of cardiovascular disease. [100] The European Cardiovascular Society's recommendations recognize that higher thresholds should be used in patients with CKD. In the majority of cases, troponin elevation can not be attributed solely to renal failure and should not be trivialized [101]. It is proposed to compare measured troponin values with older values, and integrate the clinical and electrocardiographic context into the interpretation of the test. On the other hand, echocardiography can play an important role if the diagnosis of NSTEMI is not clear, by identifying potential segmental kinetic disorders or on the contrary arguments in favor of an alternative diagnosis (right ventricular overload on pulmonary embolism, pericardial effusion, aortic dissection, aortic stenosis ...). Depending on the clinical setting, other non-invasive cardiological investigations may be requested.

4. CONCLUSION

The measures for cardioprotection are part of a comprehensive and integrated strategy for the treatment of chronic uremia [97]. They are now applicable to all dialysis and transplant patients, given the impact of cardio-vascular comorbidity on the survival of these patients [97,98]. They are also required as early as the pre-dialysis stage of CKD, in combination with measures for nephroprotection. This complex treatment requires the intervention of the nephrologist and the cardiologist at the same time.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

HUMAN AND ANIMAL RIGHTS

No Animals/Humans were used for studies that are base of this research.

CONSENT FOR PUBLICATION

Not applicable.

AVAILABILITY OF DATA AND MATERIALS

The authors confirm that the data supporting the findings of this research are available within the article.

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CONFLICT OF INTEREST

The author declares that he has no conflict of interest.

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