Chronic Kidney Disease and Cardiovascular Disease: A Case Presentation

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Cardiovascular disease (CVD), the leading cause of death in the general U.S. population, is also widespread among individuals with end stage renal disease (ESRD). It is, in fact, the leading cause of mortality in this group, accounting for approximately 50% of all deaths (Ikizler, 2002). As early as the 1970s, individuals on dialysis have been recognized as having an accelerated rate of atherosclerosis and a 10-30 times greater CVD mortality compared to age-matched individuals in the general population (Foley, Parfrey, & Sarnak, 1998). It has more recently become apparent, however, that CVD begins to develop early in the course of chronic kidney disease (CKD) (Go, Chertow, Fan, McCulloch & Hsu, 2004). People in the earlier stages of CKD are actually far more likely to die from CVD than to progress to kidney failure and the need for renal replacement therapy (Keith, Nichols, Gullion, Brown & Smith, 2002).

This article is the third and final in a series on CVD risk factors and complications of CKD related to cardiovascular morbidity and mortality. The first article highlighted the epidemiology of CKD and provided an overview of the risk factors and complications that contribute to CVD. The second article in the series identified the pathophysiologic mechanisms by which traditional and nontraditional risk factors associated with CKD contribute to the CVD morbidity and mortality seen in individuals with CKD. This article will discuss nursing care and treatment of the patient with CKD focusing on slowing progression of kidney disease as well as to treating CKD complications and thus reducing risk factors for CVD.

Goal
Recognize and reduce exposure to both traditional and nontraditional renal-related cardiovascular risk factors in patients with chronic kidney disease (CKD).

Objectives
1. Discuss the prevalence of cardiovascular disease (CVD) in patients with CKD.
2. Identify traditional and nontraditional renal-related risk factors for development of CVD.
3. List interventions that are known to reduce the risk of CVD development in patients with CKD.

Definition of CVD
CVD, by definition, includes cardiac, cerebrovascular, and peripheral vascular diseases (National Kidney Foundation [NKF], 2005). In the dial-
ysis population, cardiac diseases have received the most attention because they are the most common cause of CVD deaths in that group. These include ischemic heart disease (IHD), coronary artery disease (CAD), cardiomyopathy, valvular heart disease, and arrhythmias. Although cardiac disease is the most common, morbidity and mortality related to cerebrovascular and peripheral vascular disease are also prevalent in CKD.

According to data from the United States Renal Data System (USRDS) (2001), the prevalence of coronary artery disease (CAD) and congestive heart failure (CHF) were each higher than 40% in persons on dialysis. In addition, a USRDS study examining comorbidity data in approximately 4,000 patients on dialysis demonstrated that all types of CVD were only slightly less prevalent at initiation of dialysis than in patients who were already receiving renal replacement therapy (RRT) (USRDS, 1997), suggesting that CVD may actually begin to develop early in the course of CKD. More recent data (USRDS, 2006) continues to show a similar prevalence of all types of CVD in patients with and without diabetes who have survived 1 year after initiation of renal replacement therapy. Several studies have shown, for instance, that the prevalence of left ventricular hypertrophy (LVH) is much higher in the early stages of CKD (27%-31%), when compared to similar age groups in the general population, where it is less than 20% (Foley et al., 1995; Foley & Parfrey, 1997). The prevalence of LVH increases with each progressive stage of CKD, reaching 75% by the need for initiation of RRT (Levin, 2003). Research has also suggested that even mild CKD is associated with increased risk for CAD and stroke and that this risk intensifies as CKD advances. The risk of cardiac events such as myocardial infarction (MI), for instance, has been shown to be 3.5-50 times higher in patients with Stage 5 CKD than in the general population (Sarnak & Levy, 2000). Another gripping statistic is that at least 35% of patients with CKD have evidence of an ischemic event, such as an MI or angina, at the time of initial referral to a nephrologist (Levin, 2003).

Assessment and management of risk factors and end organs damage are fundamental in the management of CVD in all individuals. A comprehensive assessment, including history and physical exam, should be completed prior to initiation of any risk-reduction or treatment interventions. Although there are many similarities between the management of CVD in the patient with CKD and other individuals, there are special considerations for both evaluation and treatment in persons with CKD (NKF, 2005).

**Assessment of Risk Factors for CVD**

Patients with CKD have many of the traditional risk factors for CVD, including older age, hypertension, dyslipidemias, diabetes mellitus, and physical inactivity (Menon, Gui, & Sarnak, 2005). Age is the only one of these traditional risk factors, shared by many patients with CKD, that is not modifiable. Other nonmodifiable CVD risk factors include gender, family history, and hereditary factors such as race. Hypertension, dyslipidemias, diabetes mellitus, smoking, and physical inactivity, risk factors that adversely affect other risk factors, such as obesity and hypertension, can all be managed or treated, thus are considered modifiable risk factors (Grundy et al., 1999).

In addition to traditional CVD risk factors, individuals with CKD must also be assessed for nontraditional risk factors. Many of the complications of CKD, when not adequately treated, may lead not only to more rapid progression of kidney disease but, also, to increased cardiovascular morbidity and mortality (NKF, 2005). These unique CKD-related risk factors for the development of CVD include anemia, proteinuria/microalbuminuria, disturbances of mineral metabolism, extra-cellular volume overload, malnutrition, inflammation, elevated homocysteine levels, and elevated c-reactive protein levels (Abramson, Jurkowitz, Vaccarino, Leventrub & McClellan, 2003; Cullerton et al., 1999; Sarnak et al., 2003; Shlipak, Fried, Stehman-Breen, Siscovick, & Newman, 2004). The Kidney Disease Outcome Quality Initiative (K/DOQI) Guidelines recommend consideration of all of these unique risk factors and suggest that efforts to reduce CVD risk should be initiated early in the course of CKD to reduce morbidity and mortality (NKF, 2005). Once the patient has been assessed for these traditional and nontraditional CVD risk factors, measures for risk factor reduction should be initiated based on the results. The interventions to achieve the above treatment goals are discussed in more detail in this case study presented later in this article.

**Evaluation and Management of CVD in Patients with CKD**

There are guidelines available to direct the practitioner in reducing a patient's cardiovascular risk factors. The National High Blood Pressure Education Program of the NIH presented its Seventh Report of the Joint National Committee (JNC) on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure in 2004 (USDHHS, 2004). Like its predecessors, these JNC 7 Guidelines provide an evidence-based approach to the prevention and management of hypertension, a major risk factor in the development of CVD as well as CKD (Chobanian et al., 2003).

The American Heart Association (AHA) Guidelines for Primary Prevention of Cardiovascular Disease and Stroke: 2002 Update: Consensus Panel Guide to Comprehensive Risk Reduction for Adult Patients without Coronary or Other Atherosclerotic Vascular Diseases provides a framework to assist primary care providers in assessment, management, and follow-up of patients who may be at risk for but who have not yet manifested cardiovascular dis-
ease (Pearson et al., 2003). Although the JNC 7 Guidelines and the AHA guidelines provide a framework for comprehensive care for the general population of patients at risk for CVD, they do not specifically address all of the CKD-related nontraditional CVD risk factors.

The Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (ATP III) Executive Summary was released in 2001 [ATP III, 2001]. Based on the ATP I and APT II, these were updated, evidenced-based clinical guidelines. They provided direction for cholesterol testing and management that expanded the indications for intensive cholesterol-lowering therapy in clinical practice and applied findings from the most recent clinical trials. While ATP III maintained attention to intensive treatment of patients with CHD, its major new feature was a focus on primary prevention in persons with multiple risk factors. Because of the focus on individuals with multiple CHD risk factors, the guidelines can be applied to the population of patients with CKD. However, they do not specifically address this group or CKD-related risk factors.

In 2005, in an effort to more effectively address the risk of CVD in patients with CKD, the National Kidney Foundation (NKF) developed the K/DOQI Guidelines for Cardiovascular Disease in Dialysis Patients (NKF, 2005). The K/DOQI Guidelines recommend that CVD risk factor reduction should be initiated early to reduce morbidity and mortality associated with CKD. The guidelines for treatment and prevention are specific to individuals with Stage 5 CKD, and the extent to which they can be applied to persons in the earlier stages is unclear.

In planning and providing care for individuals along the continuum of CKD, nephrology nurses would be best served by referring to the ANNA Nephrology Nursing Standards of Practice and Guidelines for Care (Barrows-Hudson & Prowant, 2005), which provide a framework for nursing care of the CKD patient in all stages of the disease. These guidelines include a new section on CKD Stages 1-4 and are based on and supported by the most current evidence available as well as on expert nephrology nursing opinion and practice. The following case study will examine the required nursing assessment and treatment to slow progression of CKD and to reduce CVD morbidity and mortality.

**Strategies to Slow Progression of CKD and Reduce Risk of CVD**

As previously discussed, many treatment strategies have proven to not only slow the progression of CKD but also reduce the risk of CVD development. This section will discuss treatment of Mr. X and modifications of his traditional cardiac risk factors including antihypertensive therapy, lifestyle modification, strict glycemic control, and treatment of dyslipidemias. Kidney disease related risk factors for CVD including reduction of proteinuria, correction of anemia, and treatment of disorders of bone metabolism will also be addressed. We will examine the case of Mr. X as he is followed in the CKD clinic over the course of several months. Focus on the integration of research, clinical guidelines, and nursing practice standards into the care and education of Mr. X towards efforts to reduce his CVD risk factors.

**Case Study**

Mr. X is a 57 year-old, Caucasian male with a history of Type 2 diabetes mellitus, hypertension, hyperlipidemia, and obesity. The primary care physician (PCP) and the staff of the Diabetes Care Center (DCC) have followed him over the course of several years. At his most recent visit with the PCP, Mr. X was told that he had CKD caused by his diabetes and hypertension. The PCP explained that at Stage 3 CKD, it is recommended that he see a nephrologist for evaluation and treatment. At Mr. X's appointment with the nephrologist he learns that his kidney disease is progressing because his diabetes and hypertension are not optimally controlled. He learns that he has other risk factors for progression of his CKD. The nephrologist explains that the goal of the nephrology team is to work with him and his family, the PCP, and the DCC staff to slow the rate of progression of his kidney disease.

Mr. X arrives for his first follow-up visit with the nephrology nurse practitioner (NP) after having been seen by the nephrologist. The NP allays Mr. X's immediate fear that he is nearing dialysis. The NP reinforces the goal of treatment, that is, to slow the progression of the kidney disease. The NP also begins discussion of the increased risk of developing CVD when you have CKD and explains that many of the treatments to reduce the risk of CKD will also reduce his cardiovascular risk (Go et al., 2004; NKF, 2004; NKF, 2005). Mr. X expresses frustration that he has “so many risk factors” for CVD, including diabetes mellitus, hyperlipidemia, obesity, and hypertension. The NP explains that targeting the multiple risk factors with an intensified approach, including lifestyle modification and pharmacologic treatment, can result in reduced risk of CVD by as much as 50% (Gaede et al., 2003).

**Hypertension**

The assessment and physical exam of Mr. X. reveals the following: weight 100 kg, body mass index (BMI) 31, BP 170/70 mmHg, pulse 72, respirations 16, cardiac – regular rate and rhythm, lungs – clear to auscultation, and 2+ pre-tibial edema. Mr. X’s laboratory results are as follows: blood urea nitrogen (BUN) 45 mg/dL, serum creatinine (SCR) 3.0 mg/dL, estimated glomerular filtration rate (eGFR) 42 mL/min/1.73m², hemoglobin (Hgb) 10.2 g/dL, and urine protein/creatinine ratio 1.2 g/g. The NP talks with Mr. X, and together they decide to focus on Mr. X’s hypertension. His initial BP is elevated significantly above the target and
poses both a risk for development of CVD and progression of CKD (Chobanian et al., 2003; NKF, 2002). The NP tells Mr. X that the target BP is less than 130/80 mmHg (NKF, 2004) (see Table I). The NKF-K/DOQI Clinical Practice Guidelines on Blood Pressure Management and Use of Antihypertensive Agents in Chronic Kidney Disease (NKF, 2004) state that the goals of antihypertensive therapy are to lower BP, slow the progression of kidney disease, and reduce the risk of CVD. The NP explains that the risk of death from CVD doubles for every 20 mmHg increase in systolic BP or every 10 mmHg increase in diastolic BP above usual BP of 115/75 mmHg (Leavitt, Clarke, Qzilbash, Peto, & Collins, 2002). Mr. X expresses some resistance to the lower BP target but the NP further explains that most adverse cardiovascular events take place in patients with mild or moderate BP elevations as opposed to those with more severe hypertension (Kannel, 2000). The NP emphasizes that improved BP control is one of the best ways to slow the progression of his CKD and that because of his multiple risk factors and evidence of end organ damage, he has much to gain (Giles et al., 2005).

Lifestyle Modification

Antihypertensive therapy includes lifestyle modifications, followed by pharmacological therapy (Chobanian et al., 2003; NKF, 2004). Lifestyle modifications form the cornerstone for treatment of hypertension. Table 2 presents the JNC 7 recommendations for therapeutic lifestyle changes that have shown to lower BP (Chobanian et al., 2003). On questioning Mr. X, he states he has had multiple discussions of lifestyle modifications with his PCP and at the DCC. Mr. X and the NP begin with a discussion of diet. Mr. X states that he and his wife attempt to follow the DASH (Dietary Approaches to Stop Hypertension) eating plan as he understands that studies have shown it to reduce BP (Appel et al., 1997; Harsha et al. 1999). The NP questions Mr. X further and he explains that the DASH eating plan is low in saturated fats, cholesterol, and total fats and emphasizes fruits, vegetables and low-fat milk. It includes whole grains products and limits red meats and concentrated sweets (Chobanian et al., 2003). He also claims adherence to the ADA diabetic diet and the sodium restriction, although he admits he has a fondness for “fast foods.” The NP reinforces the sodium restriction and points out to Mr. X that there is evidence that sodium retention plays a major role in hypertension in persons with CKD. The mechanism appears to be an expansion of extracellular fluid volume (Vasavada & Agarwal, 2003). In view of his edema, they also review his fluid intake and restriction. The NP instructs Mr. X to limit sodium intake to less than 2.4 g/day and limit fluid intake to 500 cc above the previous day’s output (NKF, 2002).

Diet recommendations for Mr. X and other patients with multiple diagnoses are complex. Mr. X must limit certain foods based on the diagnosis of diabetes, obesity, hyperlipidemia, and Stage 3 CKD. Briefly, restrictions are recommended for protein, total fat and saturated fats, cholesterol, phosphorous, potassium and sodium (NKF, 2004). Mr. X is referred to a diettian to help him to achieve the many dietary recommendations.

Weight reduction is also important for Mr. X who states he understands that his obesity and sedentary lifestyle are affecting his health. Patients who do not meet the recommended body weight (BMI 18.5-25.9) should be encouraged to begin a weight-loss program that promotes healthy behaviors to lose weight and maintain the loss over time. Mr. X expresses a desire to begin an exercise program to assist him with his weight loss goals. The NP encourages Mr. X and explains that obesity is a risk factor for progression of CKD and development of CVD (Kannel, LeBauer, Dawber, & McNamara, 1967; Kramer et al., 2005). In addition to reducing body weight and fat, the NP explains that the health benefits of exercise are many including reducing blood pressure, decreasing insulin resistance and glucose intolerance, raising HDL cholesterol, and lowering triglycerides. Exercise thus helps prevent and treat many of the risks factors for CVD (Thompson et al., 2003). However, because of Mr. X’s many identified CVD risk factors, a referral is made to a cardiologist for evaluation prior to the initiation of an exercise program (Fletcher et al., 1996).

In spite of his attempts at lifestyle modifications, Mr. X has required pharmacological intervention to control and treat his hypertension. Most patients with CKD will require treatment with 2 or more drugs to control hypertension (NKF, 2004). As recommended by the JNC 7 Guidelines (Chobanian et al., 2003) and the K/DOQI Clinical Practice Guidelines on Blood Pressure Management and Use of Antihypertensive Agents in Chronic Kidney Disease (NKF, 2004), Mr. X was started on an angiotensin converting enzyme (ACE) inhibitor by his PCP. An ACE inhibitor or angiotensin receptor blocker (ARB) should be used in patients with diabetic renal disease as the initial drug of choice (see Table I). Both drugs have proven to lower BP, reduce proteinuria, slow the progression of kidney disease, and reduce cardiovascular risk (Bakris & Weir, 2000; Kjeldsen & Julius, 2004; Yusuf et al., 2000).

Based on the measured BP of 170/70 mmHg, the NP decides to increase Mr. X’s dose of the ACE inhibitor. Mr. X is scheduled to have a repeat lab in 1 week, including a serum creatinine, eGFR, and potassium. Because of the increased risk of complications from pharmacologic therapy in persons with CKD, there should be frequent monitoring. The NKF-K/DOQI Clinical Practice Guidelines on Blood Pressure Management and Use of Antihypertensive Agents in Chronic Kidney Disease (NKF, 2004) recommends that the blood pressure, eGFR, and serum potassium be checked before initiation and within 12 weeks of initiation or a change in dose of an ACE inhibitor, ARB and/or diuretic as these medications may cause a decrease in GFR and/or
Table 1

Summary of Recommendations on Hypertension and Antihypertensive Agents in CKD

<table>
<thead>
<tr>
<th>Population</th>
<th>BP Goal (mm Hg)</th>
<th>Preferred Agents for CKD With (or Without) Hypertension</th>
<th>Other Agents to Reduce CVD Risk and Reach Blood Pressure Targets</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetic Kidney Disease</td>
<td>less than 130/80</td>
<td>ACE inhibitor or ARB</td>
<td>Diuretics preferred, then BB or CCB</td>
</tr>
<tr>
<td>Nondiabetic kidney disease with spot urine total protein-to-creatine ratio &gt; 200 mg/g</td>
<td>less than 130/80</td>
<td>ACE inhibitor or ARB</td>
<td>Diuretics preferred, then BB or CCB</td>
</tr>
<tr>
<td>Nondiabetic kidney disease with spot urine total protein-to-creatine ratio &lt; 200 mg/g</td>
<td>less than 130/80</td>
<td>None preferred</td>
<td>Diuretic preferred, then ACE inhibitor, ARB, BB, or CCB</td>
</tr>
<tr>
<td>Kidney Disease in the Transplant Recipient</td>
<td>less than 130/80</td>
<td>None preferred</td>
<td>CCB, diuretic, BB, ACE inhibitor, ARB</td>
</tr>
</tbody>
</table>

**Abbreviations:** ACE - angiotensin converting enzyme, ARB - angiotensin receptor blocker, BB – beta blocker, CCB – calcium channel blocker


Table 2

Lifestyle Modifications to Manage Hypertension

<table>
<thead>
<tr>
<th>Modification</th>
<th>Recommendation</th>
<th>Approximate Systolic BP Reduction Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight reduction</td>
<td>Maintain normal body weight (BMI 18.5 – 24.9)</td>
<td>5-20 mm Hg/10-kg weight loss</td>
</tr>
<tr>
<td>Adopt DASH eating plan (CKD Stage 1 – 2 only)*</td>
<td>Consume a diet rich in fruits, vegetables, and low-fat dairy products with a reduced content of saturated and total fat</td>
<td>8-14 mm Hg</td>
</tr>
<tr>
<td>Dietary sodium reduction</td>
<td>Reduce dietary sodium intake to no more than 100 mEq/L (2.4 g sodium or 6 g sodium chloride)</td>
<td>2-8 mm Hg</td>
</tr>
<tr>
<td>Physical activity</td>
<td>Engage in regular aerobic physical activity such as brisk walking (at least 30 minutes per day, most days of the week)</td>
<td>4-9 mm Hg</td>
</tr>
<tr>
<td>Moderation of alcohol consumption</td>
<td>Limit consumption to no more than 2 drinks per day (1 oz or 30 mL) ethanol in most men and no more than 1 drink per day in women and lighter-weight persons</td>
<td>2-4 mm Hg</td>
</tr>
</tbody>
</table>

**Abbreviations:** BMI - body mass index calculated as Weight in kilograms divided by the square of the height in meters; BP - blood pressure; DASH - Dietary Approaches to Stop Hypertension


* The K/DOQI recommendations differ only in the area of diet. The DASH diet is recommended for patients with CKD in Stages 1 and 2. In Stages 3-5 however, modifications in the diet are necessary due to the possibility of hyperkalemia with a diet rich in fruit and vegetables and hyperphosphatemia with low fat dairy products (Table XII). A dietary consult will be helpful in assisting the patients to meet the dietary recommendations and modifications required by CKD.
changes in potassium levels. Follow-up monitoring should be performed every 4 weeks or more frequently in patients with systolic BP less than 120 or greater than 140 mm Hg or higher, GFR less than 60 mL/min/1.73m², or if there is a change in GFR greater than 15% in 2 months (NKF, 2004).

Mr. X’s labs are reported to the office nurse: creatinine 3.3 mg/dL and potassium 4.8 mEq/L. Mr. X expresses some concern about the increase in the SCr. The nurse notes that the SCr has increased only 10% and explains to Mr. X that an increase in serum SCr of 20% - 30%, which then stabilizes, is acceptable. In fact, patients who remain on an ACE inhibitor with increases of SCr up to 30% from baseline (up to 3 mg/dL) within the first 4 months of initiation of any ACE inhibitor, had a slower rate of decline in renal function after 3 or more years (Bakris & Weir, 2000). If Mr. X were to experience a greater than 30% increase on repeated measures of SCr or show a progressive increase, the drug would be discontinued. Although hyperkalemia may also be associated with the use of an ACE inhibitor, ABP or increase in dose, the nurse notes that Mr. X’s potassium remains within the normal limits (Palmer, 2003).

After 2 weeks, Mr. X reports to the office for a blood pressure measurement. The blood pressure is now 150/82 mmHg and Mr. X expresses some frustration that his BP is not lower. The nurse explains that even small reductions in BP will decrease CVD risks (Staessen, Wang, & Thijs, 2003). In assessment of the patient, the office nurse notes the patient still has 2+ pedal edema. The nurse calls the nephrologist, who decides to start Mr. X on a diuretic. As monotherapy rarely achieves BP goals in patients with CKD who are hypertensive, a second or third agent is often required. The nurse explains to Mr. X that extracellular (ECF) volume overload is a manifestation of CKD, that occurs when the reduction in GFR leads to decreased renal excretion of sodium and water.

Notwithstanding the absence of peripheral edema, patients with CKD can, even early in the course of the disease, experience a 10%-30% increase in ECF volume (Wilcox, 2002). This chronic ECF volume overload can lead to LVH and, possibly, to inflammatory activation (London & Parfrey, 1997; Pecoiits-Filho et al., 2004). Diuretics are an ideal second drug and potentiate the BP-lowering effects of an ACE inhibitor and/or ARB (NKF, 2004). Thiazide-type diuretics have been the basis of antihypertensive therapy in most outcome trials. Their use is associated with decreased CVD (Chobanian et al., 2003). As Mr. X’s CKD progresses, he may be changed to a loop diuretic as diazide diuretics may become ineffective in patients with GFR less than 30 mL/min/1.73m². The nurse tells Mr. X to call and report dizziness, light-headedness, cramping, weakness or any new symptoms if they occur before his next appointment. Electrolyte abnormalities, including hypomagnesemia, hypotension, hypokalemia, and volume depletion, are all potential side effects and patients should be monitored for these (Wilcox, 2002).

**Proteinuria**

Proteinuria or microalbuminuria, a form of proteinuria that is the earliest sign of CKD in individuals with diabetes, is linked to an increased prevalence of CKD risk factors, including HTN, dyslipidemias, and poor glucose control (NKF, 2006). The K/DOQI guidelines (NKF, 2004) recommend that proteinuria be monitored as it is known to increase risk of CKD progression and is a CVD risk factor (Jafar et al., 2004; Klausen et. al, 2004). In fact, the predictive power of urinary protein for CV risk is independent of other risk factors, including level of kidney function and hypertension (Hillege et al., 2002; Klausen et al. 2004). In addition to monitoring Mr. X’s BP response to therapy, his level of proteinuria will be monitored in order to initiate or increase antihypertensive agents known to reduce proteinuria, including ACE inhibitors, ARBs, and beta blockers. The NP explains to Mr. X that the second goal of antihypertensive therapy is to reduce urinary protein excretion to less than 500 mg/day. Studies have shown long-term favorable impact on kidney disease progression when there is a reduction in proteinuria (Hunsicker et al., 1997; Ruggenenti, Perna, & Remuzzi, 2003). Studies have shown a combination of ACE inhibitor and ARB significantly improves BP control and further reduces albuminuria (Campbell et al., 2003; Morgensen et al., 2000; Nokoa, et al., 2003).

The NP explains that albuminuria or proteinuria can be measured in a 24-hour urine or from an untimed spot urine sample. The random-spot urine measurement of the albumin or protein-to-creatinine ratio is now more widely utilized due to the difficulty in collecting an accurate 24-hour specimen. In the measurement of a spot urine albumin-to-creatinine ratio, microalbuminuria is defined as a ratio between 17–250 mg/g in males and 25–355 mg/g in females and albuminuria, as a ratio greater than 250 mg/g in men and 355 mg/g in women. When albumin excretion exceeds 500-1000 mg/g as measured in a spot albumin-to-creatinine ratio, it is acceptable to measure protein-to-creatinine ratio due to cost and technical difficulty in measuring albumin (NKF, 2002). Mr. X is scheduled to have an untimed spot urine sample at each monthly lab appointment.

The following month Mr. X achieves the blood pressure target of 120/60 mmHg while maintaining a less than 30% increase in serum creatinine. His potassium is controlled within the normal range with diet and Mr. X’s urine protein/creatinine ratio has fallen to 432 mg/g. He has been evaluated by the cardiologist with a stress test and has started an exercise program.

**Hyperglycemia**

Having achieved successful BP control and reduction in proteinuria with lifestyle modifications and medications, Mr. X is anxious to concen-
trate on other ways to slow progression of his CKD and further reduce his cardiovascular risk. The NP explains to Mr. X that he has already been working on a second risk factor, hyperglycemia (DCCTRG, 1993; UKPDS, 1998). Mr. X has been working with the DCC staff on improving his glucose control. Mr. X’s most recent HbA1c is 6.3%. He checks his blood sugars twice per day and reports blood sugars in the 90-130 mg/dL range. The American Diabetes Association (ADA) through its Clinical Practice Recommendations (2006), provides the following goals for treatment of patients with diabetes: glycosylated hemoglobin (HbA1c) less than 7.0%, a preprandial plasma glucose of 90–130 mg/dL, and peak postprandial plasma glucose of less than 180 mg/dL. The cornerstone of glycemic control is also lifestyle modification, including dietary control, weight loss, and exercise (ADA, 2006).

The NP asks Mr. X if he has had any hypoglycemic episode and explains to him potential problems in the treatment of patients with diabetes and kidney disease can occur with drugs used to treat hyperglycemia. Mr. X expresses some frustration that his blood sugar was very well controlled but the nephrologist advised the DCC to stop the metformin and he is now worried that the HbA1c will increase. The NP explains that the metformin, although one of the most widely prescribed oral antidiabetic agents in the country, was discontinued due to his CKD. Patients who have a GFR less than 40 mL/min/1.73m² have the risk of developing life-threatening lactic acidosis if metformin therapy is continued (Wolf & Ritz, 2003). The NP explains that with careful monitoring Mr. X will be able to achieve the target glycates. Patients with diabetes and CKD must be followed closely to achieve optimal HbA1c target while avoiding hypoglycemic risks. Co-management of patients with diabetes with a diabetes team may assist in achieving treatment goals (ADA, 2004).

**Dyslipidemias**

On the next visit Mr. X’s labs include a fasting lipid panel with the following results: total cholesterol 250 mg/dL, LDL 130 mg/dL, HDL 30 mg/dL and triglycerides 205 mg/dL. The NP explains to Mr. X that reducing lipid levels will not only improve his CV outcomes but treatment of dyslipidemias has been shown to slow the progression of CKD (ATP III, 2001; Freid, Orchard, & Kasiske, 2001). The NKF-K/DOQI Guidelines recommend that clinicians treating patients with CKD in Stages 1-4 should follow the Adult Treatment Panel Guidelines (ATP III, 2001) as adopted for patients with CKD and found in Table 3 (NKF, 2003b).

If patients do not reach their goals with therapeutic lifestyle changes, which includes lowering of saturated fats, increasing fiber intake (especially viscous fiber), glycemic control, weight management, increased physical activity, moderation in alcohol consumption and smoking cessation, then drug therapy should be initiated. HMG CoA reductase inhibitors, nicotinic acid, bile acid sequestants, fibric acids, and combination can be used to reach lipid goals (ATP III, 2001; NKF, 2003b). Mr. X is started on an HMG CoA reductase inhibitor.

**Smoking Cessation**

At the same visit, the NP notes that Mr. X is wearing a nicotine patch. The NP gives Mr. X positive feedback and explains to him that according to the American Heart Association (AHA), as many as 30% of all coronary heart disease deaths in the United States are attributable to cigarette smoking, and smoking nearly doubles the risk of ischemic stroke (Ockene & Miller, 1997). In fact

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**Table 3**

<table>
<thead>
<tr>
<th>Dyslipidemia</th>
<th>Goal</th>
<th>Initiate</th>
<th>Increase</th>
<th>Alternative</th>
</tr>
</thead>
<tbody>
<tr>
<td>TG ≥ 150 mg/dL</td>
<td>TG &lt; 150 mg/dL</td>
<td>TLC</td>
<td>TLC + Fibrate or Niacin</td>
<td>Fibrate or Niacin</td>
</tr>
<tr>
<td>LDL ≥ 100 -129 mg/dL</td>
<td>LDL &lt; 100 mg/dL</td>
<td>TLC</td>
<td>TLC + low dose Statin</td>
<td>Bile acid seq. or Niacin</td>
</tr>
<tr>
<td>LDL ≥ 130 mg/dL</td>
<td>LDL &lt; 100 mg/dL</td>
<td>TLC + low dose Statin</td>
<td>TLC + max dose Statin</td>
<td>Bile acid seq. or Niacin</td>
</tr>
<tr>
<td>TG ≥ 200 mg/dl and non-HDL ≥ 130 mg/dl</td>
<td>Non-HDL &lt; 130 mg/dL</td>
<td>TLC + low dose Statin</td>
<td>TLC + max dose Statin</td>
<td>Fibrate or Niacin</td>
</tr>
</tbody>
</table>

**Abbreviations:** TG - triglycerides; LDL - low-density lipoprotein cholesterol; HDL - high-density lipoprotein cholesterol; TLC - therapeutic lifestyle changes

according to the Multiple Risk Factor Intervention Trial (MRFIT), smoking is one of the leading risk factors for ESRD (Orth, 2004). Smoking cessation treatments that have been found to be safe and effective include counseling and medications (nicotine gum, inhaler, nasal spray, patch, and lozenge and bupropion or a combination of both) (Fiore, 2000).

C-Reactive Protein

Mr. X asks the NP about the “CRP level” that was drawn by the cardiologist. The NP explains that the high sensitivity C-reactive protein (hs-CRP) is a biomarker that may be predictive of future MI, stroke and CV death ( Ridker, Cushman, Stamper, Tracy & Hennekens, 1997). The nurse explains that an elevated CRP should be rechecked and that the average of the two laboratory findings could be helpful in further defining his risk for CVD. According to the AHA measurement, the CRP may be useful as part of a global coronary risk assessment in adults with intermediate CV risks (Pearson et al., 2003).

CKD-Related CVD Risk Factors

Many of the complications of CKD, which can be prevented or delayed by earlier detection and appropriate evaluation and management, are also cardiovascular risk factors. As we continue to follow and treat Mr. X, the following complications of CKD, anemia and disorders of calcium and phosphorus metabolism, will be discussed. 

Anemia. Mr. X’s initial Hgb, 10.3 g/dL, showed that Mr. X is anemic. At the second visit Mr. X complains of low energy, fatigue, inability to concentrate, gastrointestinal symptoms and decreased quality of life. He feels that his symptoms are related to the increase in blood pressure medication. The NP explains to Mr. X that his symptoms are probably related to his anemia (NKF, 2006). The NP tells Mr. X that anemia is a complication of CKD, which commonly presents in Stage 3 CKD. Mr. X’s stage (NKF, 2006). Mr. X states he feels better knowing there is a cause for his symptoms. The NP explains that his anemia is most likely due to erythropoietin deficiency and after some additional testing and improved control of his hypertension, treatment with an erythropoietin stimulating agent (ESA) agent will begin. Treatment will also include iron and vitamin supplementation. The treatment goals as recommended by the K/DOQI Guidelines are to maintain a Hgb greater than 11.0 g/dL. (NKF, 2006). The NP further explains that anemia, if left untreated, is a risk factor for LVH, fatal CHD, and increased stroke mortality. (Abramson et al., 2003; Astor, Coresh, Heiss, & Saranak, 2006; Levin et al., 1999; Viagopoulos et al., 2005).

Disorders of bone and mineral metabolism. At a subsequent visit Mr. X notes a new result on his laboratory report, the intact parathyroid hormone (iPTH) level. The NP explains that disturbances of mineral metabolism are common in individuals with CKD. Such metabolic disorders as elevated calcium, phosphorus, and parathyroid hormone (PTH) levels can occur early in the course of CKD and have all independently been linked with cardiac death in individuals undergoing dialysis (Ganesh, Stach, Levin, Hylbert- Shearson & Port, 2001). The NP explains the K/DQOI Clinical Practice Guidelines for Bone Mineral Metabolism and Disease in CKD (2003a) recommend at least annual measurement of serum calcium, phosphorus, and PTH levels beginning at Stage 3 CKD. The NP explains to Mr. X that excess PTH, a complication of CKD, is linked not only to bone disease but also to non skeletal tissue deposition in the heart and cardiovascular system and that treatment is essential to reduce CVD risk (Goodman et al., 2004). The NP explains that the goals of treatment of secondary hyperparathyroidism (SHPT) include prevention of hyperphosphatemia, maintenance of normal serum calcium levels, treatment of vitamin D deficiency, and suppression of PTH (NKF, 2003a).

As reduced phosphate levels very early in CKD have shown to result in decreased development of SHPT, the NP begins with a discussion for the first steps in preventing hyperphosphatemia, dietary restriction of phosphate, and phosphate binders that prevent its absorption (NKF, 2003a; Slatapolsky, Brown, & Drusso, 2001). Dietary phosphate restriction is a challenge, as eating enough protein to prevent malnutrition can result in an overload of phosphorus. Calcium-based phosphate binders and non-calcium-based phosphate binders are effective in lowering serum phosphorus levels in patients with GFR less than 60 mL/min/1.73m2 (NKF, 2003a). Total elemental calcium intake (dietary intake plus supplemental calcium) should not exceed 2000 mg/day. Target treatment goals for calcium and phosphorus are a calcium level of 8.4–9.5 mg/dL in CKD Stages 3-5 and a phosphorus of 2.7–4.6 mg/dL in CKD Stages 3-4 (NKF, 2003a). Finally, the NP emphasizes the importance of lower phosphorus levels, telling Mr. X that levels greater than 3.5 g/dL are associated with increased mortality in patients with CKD (Kestenbaum et al., 2005).

Mr. X’s iPTH level is 95 pg/mL. The NP explains that the target for iPTH for patients in Stage 3 CKD is 35–70 pg/mL and for patients with Stage 4 CKD the level is 70–110 pg/mL. If PTH levels exceed these targets, then vitamin D (serum 25 hydroxyvitamin D) should be measured and if levels are low, then oral vitamin D3 (ergocalciferol) is initiated. If the level of vitamin D3 is not low, then treatment with an active oral vitamin D sterol is indicated. The NP explains to Mr. X that his calcium, phosphorus, and PTH levels will be monitored closely during therapy with the phosphate binders, vitamin D, and vitamin D sterols (NKF, 2003a).

Conclusion

It is clear that CVD risk factor reduction should begin early. At the start of renal replacement therapy, 40% of the patients have coronary...
Table 4
Strategies to Slow Progression of CKD and CVD

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Target/Treatment Recommendations</th>
<th>Nursing Considerations</th>
</tr>
</thead>
</table>
| Hypertension | • Target: less than 130/80 mmHg  
• ACE inhibitor/ARB preferred in patients with diabetes and patients with protein-to-creatinine ratio greater than 200 mg/g.  
• All antihypertensive agents effective in patients without diabetes and protein-to-creatinine ratio less than 200 mg/dL. Follow recommendations of JNC 7 for drug selection in other comorbidities.  
• Diuretics are ideal second drug (thiazides may not be effective at GFR less than 40 mL/min/1.73m²)  
• Fluid restriction and sodium restriction critical.  
• Initiate TLC (weight reduction, DASH diet, decreasing dietary sodium, increasing physical activity, alcohol moderation)  
• Side effects of ACE inhibitor or ARB include hyperkalemia and decreasing GFR (increasing SCr).  
• ACE inhibitors can cause angioedema and cough.  
• Monitor for hypotension with all agents.  
• Monitor for electrolyte abnormalities with diuretics.  
| Proteinuria | • Target: less than 500 mg - 1 g/24 hour  
• ACE inhibitor and ARB effective in reducing proteinuria. Combination may have increased effect.  
• Monitor urine protein-to-creatinine ratio for improvements.  
• Side-effects of ACE inhibitor/ARB listed above.  
| Hyperglycemia | • Targets:  
HbA1c less than 7.0%  
Preprandial glucose: 90-130 mg/dL  
Peak postprandial glucose less than 180 mg/dL  
• Diabetes self-management education essential  
• Monitor patients for side effects: hypoglycemia, weight gain and edema.  
• Avoid Metformin due to development of lactic acidosis GFR less than 40 mL/min/1.73m²  
| Hyperlipidemia | • Targets:  
LDL less than 100 mg/dL  
Non-HDL less than 130 mg/dL  
Trig. less than 150 mg/dL  
HDL greater than 40 mg/dL (varies by gender)  
• TLC + Statin recommended.  
• Fibrate and Nicin as needed.  
• Monitor patients for rhabdomyolysis and increased LFTs with statin.  
• Fibrates renally excreted, use lower doses.  
| Smoking | Target: Cessation of Smoking  
• Counseling, Nicotine replacement, bupropion are effective.  
• Address cessation at every encounter.  
| Nutrition | • Targets:  
HCO3 greater than 22 mg/dL  
Albumin greater than 3.5 g/dL  
K⁺ - 3.5-5.5 mEq/L  
BMI - 18.5 - 25.9  
• Protein:  
1.2 – 1.4 mg/kg/day  
0.6 – 0.8 mg/kg/day (Stage3/4)  
• Calorie:  
35 kcal/kg/day < 60 years old  
30 – 35 kcal/kg/day > 60 years old  
• Potassium: less than 2000 mg/day (based serum K⁺ level)  
• Sodium: less than 2400 mg/day  
• Calcium: less than 2000 mg/day  
• Phosphorous: less than 1000 mg/day (Stage 3/4)  
• Fluid: 500 cc + 24 hr urine output/day  
• HCO3 less than 22 mg/dL - alkali salts 0.5-1.0 meq/kg/day  
| Anemia | • Target: Hgb 11 – 12 mg/dL  
• Anemia workup: Assess RBC indices, retic ct, iron profile, B12 & folate levels  
• Initiate ESAs and target 11-12 mg/dL.  
| Bone Metabolism | • Stage 3 Targets:  
Phos. 2.7 – 4.6 mg/dL  
IPTH 35-70 pg/mL – PTH  
Ca – normal for lab  
• Stage 4 Targets:  
Phos. 2.7 – 4.6 mg/dL  
IPTH 70 – 110 pg.ml  
Ca – normal for lab  
• Stage 3 & 4 increased iPTH - Measure serum 25-hydroxyvitamin D  
< 30 ng/ml - ergocalciferol (D2)  
> 30 ng/ml - active Vitamin D  
• Increased Phos. – low phos diet/binder  
• Increased Ca – dc Ca and Vitamin D  

Abbreviations: TLC - therapeutic lifestyle changes; ACE - angiotensin converting enzyme; ARB - angiotensin receptor blocker; GFR - glomerular filtration rate; Scr - serum creatinine; JNC VII - Joint national committee on treatment of hypertension; LDL - low density lipoprotein; HDL - high density lipoprotein; LFT - liver function test; Hgb - hemoglobin; RBC - red blood cell; Retic ct - reticulocyte count; BMI - body mass index; K⁺ - potassium; HCO₃⁻ - bicarbonate, BP - blood pressure; Phos - phosphorous; Ca - calcium; iPTH - intact parathyroid hormone

Sources: ATP III, 2001; Chobanian et al., 2003; ADA 2006; National Kidney Foundation 2002-2006
heart disease and 75% of the patients have abnormal left ventricular size and function (Foley et al., 1998). Even mild to moderate kidney dysfunction is associated with increased rate of death from cardiovascular causes (Go et al., 2004; Manjunath et al., 2003; Shilpak et al., 2004). Although no prospective studies have been performed that show risk factor reduction reduces the risk of CVD in patients with CKD, most clinicians agree that the threshold for initiating cardiovascular risk factor reduction should be lower and recommend aggressive therapy to reduce risks (NKF, 2002). Cardiovascular risk factor reduction for patients with CKD includes aggressive management of hypertension, reduction of proteinuria, control of hyperglycemia, and treatment of dyslipidemias. Additionally disorders of mineral metabolism and anemia should also be managed aggressively (Sarnak et al., 2003). Nurses play a key role in the integration of research, practice guidelines, and nursing standards into clinical practice, including education of patients in the fight against the development of CVD in patients with CKD.


References


Kidney Diseases, 47(Suppl 3), S1-S145.


1. What statement is true about the development of CVD in patients with CKD?
   A. CVD has a much higher prevalence in patients on renal replacement therapy than in patients with CKD stages 2-4.
   B. Left ventricular hypertrophy (LVH) begins to develop after patients start dialysis.
   C. About 30% of patients referred to a nephrologist have evidence of angina.
   D. CVD develops early in the course of CKD.

2. Traditional modifiable risk factors for the development of both CVD and CKD include
   A. hypertension only.
   B. hypertension and diabetes mellitus only.
   C. hypertension, diabetes mellitus, and smoking only.
   D. hypertension, diabetes mellitus, smoking, and obesity.

3. Renal-related risk factors for development of CVD include
   A. anemia only.
   B. anemia and proteinuria only.
   C. anemia, proteinuria, and disturbance of mineral metabolism only.
   D. anemia, proteinuria, disturbance of mineral metabolism, and physical inactivity.

4. According to a study by Gaede and associates (2003), an intensive approach to treatment of patients with CVD can reduce risk by as much as
   A. 10%.
   B. 30%.
   C. 50%.
   D. 60%.

5. The goal of treatment of hypertension in patients with CKD includes
   A. lower BP only.
   B. lower BP and slow progression of CKD only.
   C. lower BP, slow progression of CKD, and reduce CVD risk only.
   D. lower BP, slow progression of CKD, reduce CVD risk, and decrease proteinuria.

6. The largest possible reduction in systolic BP is associated with which therapeutic lifestyle changes?
   A. DASH diet.
   B. Weight reduction.
   C. Physical activity.
   D. Moderation in alcohol consumption.

7. After starting an ACE inhibitor or ARB, it is critical to check
   A. BP in one week.
   B. potassium in 2 months.
   C. eGFR in 1-2 weeks.
   D. Urine protein/creatinine ratio in 2 weeks.

8. Metformin should be decreased in patients with CKD due to the risk of
   A. hypoglycemia.
   B. lactic acidosis.
   C. hyperlipidemia.
   D. proteinuria.

9. Anemia, if left untreated, may be a risk factor for
   A. LVH only.
   B. LVH and coronary heart disease (CHD) only.
   C. LVH, CHD, and stroke only.
   D. LVH, CHD, stroke, and hypertension.

10. Which statement is true concerning treatment of the disturbances of mineral metabolism?
    A. Total elemental calcium intake should be at least 3 g/day.
    B. Reduced phosphorous levels result in decreased development of SHPT.
    C. Active oral Vitamin D sterols are indicated for treatment of 25 hydroxyvitamin D deficiency.
    D. Only phosphorous levels greater than 4.5 g/dl are associated with increased mortality.
Chronic Kidney Disease and Cardiovascular Disease: A Case Presentation

ANNJ0708

ANSWER/EVALUATION FORM

Chronic Kidney Disease and Cardiovascular Disease: A Case Presentation
Patricia B. McCauley, MSN, RN, ACNP, CNN and Patricia B. Salai, MSN, RN, CRNP, CNN

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Evaluation

1. The objectives were related to the goal. 2. Objectives were met
   a. Discuss the prevalence of cardiovascular disease (CVD) in patients with CKD.
   b. Identify traditional and nontraditional renal-related risk factors for development of CVD.
   c. List interventions that are known to reduce the risk of CVD development in patients with CKD.
3. The content was current and relevant.
4. This was an effective method to learn this content.
5. Time required to complete reading assignment: ______ minutes.

GOAL

Recognize and reduce exposure to both traditional and nontraditional renal-related cardiovascular risk factors in patients with CKD.

I verify that I have completed this activity:

__________________________________________

(Signature)

Comments ________________________________

Suggested topics for future articles?

__________________________________________

__________________________________________