INTRODUCTION TO CHRONIC KIDNEY DISEASE (CKD)

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Academy of Family Physicians of Malaysia

Malaysian Family Medicine Specialist Association
# Table of Contents

## CHRONIC KIDNEY DISEASE (CKD)

4. Definition  
4. Pathophysiology  
5. Prevalence and incidence  
5. Age  
6. Mortality and morbidity  
6. Stages of CKD  
7. Causes of CKD  
7. Diagnosis  
8. Laboratory studies  
9. Imaging studies

## ABSTRACTS

10. Can we prolong life of patients with advanced CKD: what is the clinical evidence?  
12. Quality of life in CKD.  
13. End-stage renal disease (ESRD) preceded by rapid declines in kidney function: a case series.  
15. Drug therapy in patients with chronic renal failure.  
16. Possible link between metabolic syndrome and chronic kidney disease in the development of cardiovascular disease.


Definition

Chronic kidney disease (CKD) is a serious condition associated with premature mortality, decreased quality of life, and increased health-care expenditures. 1 CKD refers to an irreversible loss of renal function that develops due to a multifactorial etiology over a period of a few years. Initially it starts as a biochemical abnormality and progresses in stages. Earlier stages of CKD can be detected through routine laboratory measurements. Loss of renal function happens progressively leading to loss of excretory, metabolic and endocrine functions.

The Kidney Disease Outcomes Quality Initiative (KDOQI)2 of the National Kidney Foundation (NKF) defines CKD as:

1. Kidney damage for three or more months, as defined by structural or functional abnormalities of the kidney, with or without decreased glomerular filtration rate (GFR) manifest by either:
   a. Pathological abnormalities; or
   b. Markers of kidney damage, including abnormalities in the composition of the blood or urine, or abnormalities in imaging tests.

2. GFR less than 60 mL/min/1.73 m² for three or more months. Whatever the underlying etiology, the destruction of renal mass with irreversible sclerosis and loss of nephrons leads to a progressive decline in GFR. The clinical signs and symptoms of renal failure manifest during the later stages of the condition. This stage is sometimes referred to as uremia.3

Untreated CKD can result in end-stage renal disease (ESRD) and necessitate dialysis or kidney transplantation.

Pathophysiology

Approximately one million nephrons are present in each kidney, each contributing to the total GFR. Regardless of the etiology of renal injury, with progressive destruction of nephrons, the kidney has an innate ability to maintain GFR by hyperfiltration and compensatory hypertrophy of the remaining healthy nephrons. This nephron adaptability allows for continued normal clearance of plasma solutes so that substances such as urea and creatinine start to show significant increases in plasma levels only after total GFR has decreased to 50%, when the renal reserve has been exhausted. The plasma creatinine value will approximately double with a 50% reduction in GFR. A rise in plasma creatinine from a baseline value of 0.6 mg/dL to 1.2 mg/dL in a patient, although still within the reference range, actually represents a loss of 50% of functioning nephron mass.

The residual nephron hyperfiltration and hypertrophy, although beneficial for the reasons noted, has been hypothesized to represent a major cause of progressive renal dysfunction. This is believed to occur because of increased glomerular capillary pressure, which damages the capillaries and leads initially to focal and segmental glomerulosclerosis and eventually to global glomerulosclerosis. This hypothesis has been based on studies of five-sixths nephrectomized rats, who develop lesions that are identical to those observed in humans with CKD.
Factors other than the underlying disease process and glomerular hypertension that may cause progressive renal injury include the following:

- Systemic hypertension
- Acute insults from nephrotoxins or decreased perfusion
- Proteinuria
- Increased renal ammoniagenesis with interstitial injury
- Hyperlipidemia
- Hyperphosphatemia with calcium phosphate deposition
- Decreased levels of nitrous oxide
- Smoking.

**Prevalence and Incidence**

CKD is a worldwide public health problem and is now recognized as a common condition that is associated with an increased risk of cardiovascular disease and chronic renal failure (CRF). In the United States the prevalence and incidence of kidney failure treated by dialysis and transplantation have increased from 1988 to 2004. This could be due to the increasing prevalence of diabetes and hypertension. A similar trend is seen in Malaysia where diabetes is increasingly prevalent.

**Age**

CKD is found in persons of all ages. The normal annual mean decline in the GFR with age from the peak GFR (approximately 120 mL/min/1.73 m²) attained during the third decade of life is approximately 1 mL/min/1.73 m², reaching a mean value of 70 mL/min/1.73 m² at age 70 years. Nonetheless, in the United States, the highest incidence rate of ESRD occurs in patients older than 65 years. From the 3rd National Health and Nutrition Examination Survey (NHANES III) data, the prevalence of CKD was 37.8% among patients older than 70 years. Besides diabetes mellitus and hypertension, age is an independent major predictor of CKD. The biologic process of aging initiates various structural and functional changes within the kidney. Renal mass progressively declines with advancing age. Glomerulosclerosis leads to a decrease in renal weight. Histologic examination is notable for a decrease in glomerular number of as much as 30% to 50% by age 70 years.

Ischemic obsolescence of cortical glomeruli is predominant, with relative sparing of the renal medulla. Juxtamedullary glomeruli see a shunting of blood from the afferent to efferent arterioles, resulting in redistribution of blood flow favoring the renal medulla. These anatomical and functional changes in renal vasculature appear to contribute to an age-related decrease in renal blood flow.

Given the histologic evidence for nephronal senescence with age, a decline in the GFR is expected. However, a wide variation in the rate of decline in the GFR is reported because of measurement methods, race, gender, genetic variance, and other risk factors for renal dysfunction. Because of these anatomical and physiological changes, elderly patients with CKD may behave differently, in terms of progression and response to pharmacological treatment, than younger patients.
Mortality and Morbidity

CKD is a major cause of morbidity and mortality, particularly at the later stages. The 5-year survival rate for a patient undergoing chronic dialysis in the United States is approximately 35%. This is approximately 25% in patients with diabetes. The most common cause of death in the dialysis population is cardiovascular disease.

Among patients with ESRD aged 65 years and older, the mortality rates are 6 times higher than in the general population. In 2003, over 69,000 dialysis patients enrolled in the ESRD program died (annual adjusted mortality rate of 210.7 per 1000 patient-years at risk for the dialysis population, which represents a 14% decrease since peaking at 244.5 per 1000 patient-years in 1988). The highest mortality rate is within the first 6 months of initiating dialysis, which then tends to improve over the next 6 months, before increasing gradually over the next 4 years.

The mortality rates associated with hemodialysis are striking and indicate that the life expectancy of patients entering into hemodialysis is markedly shortened. At every age, patients with ESRD on dialysis have significantly increased mortality when compared with non-dialysis patients and individuals without kidney disease. At age 60 years, a healthy person can expect to live for more than 20 years, whereas the life expectancy of a 60-year-old patient starting hemodialysis is closer to 4 years.

Stages of CKD

The stages of CKD proposed by KDOQI in the table below (Table 1) is followed internationally. The table also lists the potential complications due to the reduced GFR.

**Table 1: Stages of CKD with potential complications of reduced GFR.**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
<th>GFR (mL/min/1.13m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Kidney damage⁶ with normal or ↑GFR</td>
<td>≥ 90</td>
</tr>
<tr>
<td>2</td>
<td>Kidney damage⁶ with mild ↓GFR</td>
<td>60-89</td>
</tr>
<tr>
<td>3</td>
<td>Moderate ↓ in GFR</td>
<td>30-59</td>
</tr>
<tr>
<td>4</td>
<td>Severe ↓ in GFR</td>
<td>15-29</td>
</tr>
<tr>
<td>5</td>
<td>Kidney failure</td>
<td>&lt; 15 or on dialysis</td>
</tr>
</tbody>
</table>

**Potential complications of reduced GFR**

- Anemia, including functional iron deficiency
- Calcium absorption decreases
- Hyperkalemia
- Hyperphosphatemia
- Metabolic acidosis
- BP increases
- Dyslipidemia/heart failure/volume overload
- Hyperparathyroidism
- Left ventricular hypertrophy

*The listed complications are not specific to CKD and may indicate other conditions. These complications are generally noted with the decreased GFR.

#Kidney damage is defined as demonstrated pathological findings in the kidney by biopsy or imaging studies or abnormal laboratory findings in blood or urine tests (proteinuria, albuminuria, hematuria or presence of white blood cells, casts).
The KDOQI definition and the classification of CKD allow better communication and intervention at the different stages. In stage 1 and stage 2 CKD, GFR alone does not clinch the diagnosis. Other markers of kidney damage, including abnormalities in the composition of blood or urine or abnormalities in imaging tests, should also be present in establishing a diagnosis of stage 1 and stage 2 CKD.

**Causes of CKD**

Epidemiological studies show an increased risk for CKD, especially kidney failure, among individuals with certain clinical and sociodemographic characteristics. This suggests that there are risk factors for CKD. The morbidity and mortality due to CKD could be reduced greatly by evaluating individuals with risk factors, to enable earlier detection, and management. This is more important, since CKD, by itself, does not exhibit any symptoms during the early stages and it is not practically possible to routinely screen the whole population for CKD. Monitoring the population at risk is a more feasible solution. The conditions that are termed as risk factors for development of CKD are:

<table>
<thead>
<tr>
<th>Clinical conditions</th>
<th>Sociodemographic factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td>Older age</td>
</tr>
<tr>
<td>Urinary tract infections</td>
<td>Ethnicity</td>
</tr>
<tr>
<td>Family history of CKD</td>
<td>Exposure to certain chemical and environmental conditions</td>
</tr>
<tr>
<td>Exposure to certain drugs</td>
<td>Low income/education</td>
</tr>
<tr>
<td>Hypertension</td>
<td>Autoimmune disease</td>
</tr>
<tr>
<td>Urinary stone</td>
<td>Lower urinary tract obstruction</td>
</tr>
<tr>
<td>Recovery from acute kidney failure</td>
<td>Reduction in kidney mass</td>
</tr>
<tr>
<td></td>
<td>Low birth weight</td>
</tr>
<tr>
<td></td>
<td>Systemic infections</td>
</tr>
<tr>
<td></td>
<td>Neoplasia</td>
</tr>
</tbody>
</table>

Among these risk factors, diabetes is an ever increasing threat in the Malaysian population. The number of people affected with diabetes is steadily increasing in the Malaysian population. This increasing group of diabetics will adversely increase the number of people with CKD. The costs of managing people with CKD put an enormous strain on the public health system.

**Diagnosis**

Earlier stages of kidney disease can be detected through laboratory testing. Measurement of serum creatinine and estimation of GFR can identify patients with reduced kidney function. Measurement of urinary albumin excretion can identify some, but not all, patients with kidney damage. Screening asymptomatic individuals at increased risk could allow earlier detection of CKD. Until recently, recommendations for screening for CKD in adults were largely focused on patients with hypertension due to the association of hypertension with CKD. However recent analysis of the 3rd National Health and Nutrition Examination Survey (NHANES III) database indicated that only 70% of individuals in the United States with elevated serum creatinine had hypertension.

Screening of all individuals with hypertension and diabetes with appropriate measurement and interpretation of urine albumin and serum creatinine could identify a large number of patients with earlier stages of CKD. The challenge is, in identifying the disease early, as early diagnosis and treatment can prevent progression of the condition into final stages thus preventing morbidity and mortality greatly.
Laboratory Studies

Laboratory diagnostic tests for CKD are focused on assessing the functioning level of the kidney. CKD affects other systems in the body due to the various effects caused by the excretory malfunction of the kidney. Many tests can be advised to diagnose CKD. Some of the tests also serve as an indicator for the cause or effect of CKD. The following tests may be indicated:

- **Serum electrolytes, BUN, and creatinine** - The BUN and creatinine levels will be elevated in patients with CKD. Hyperkalemia or low bicarbonate levels may be present in patients with CKD.
- **Serum calcium, phosphate, vitamin D, and intact parathyroid hormone (PTH) levels** are obtained to look for evidence of renal bone disease.
- **CBC count** - Normochromic normocytic anemia is commonly seen in CKD. Other underlying causes of anemia should be ruled out.
- **Serum albumin** - Patients may have hypoalbuminemia due to urinary protein loss or malnutrition.
- **Lipid profile** - A lipid profile should be performed in all patients with CKD because of their increased risk of cardiovascular disease.
- **Urinalysis** - Dipstick proteinuria may suggest a glomerular or tubulointerstitial problem. The urine sediment finding of RBCs, RBC casts, suggests proliferative glomerulonephritis. Pyuria and/or WBC casts are suggestive of interstitial nephritis (particularly if eosinophilia is present) or urinary tract infection.
- **Spot urine collection** for total protein-to-creatinine ratio allows reliable approximation (extrapolation) of total 24-hour urinary protein excretion. A value of greater than 2 g is considered to be within the glomerular range, and a value of greater than 3-3.5 g is within the nephrotic range; less than 2 is characteristic of tubulointerstitial problems.
- **Twenty-four hour urine collection** for total protein and creatinine clearance.

In certain cases, the following tests may be ordered as part of the evaluation of patients with CKD:

- **Serum and urine protein electrophoresis** to screen for a monoclonal protein possibly representing multiple myeloma.
- **Antinuclear antibodies (ANA), double-stranded DNA antibody** levels to screen for systemic lupus erythematosus.
- **Serum complement levels** - May be depressed with some glomerulonephritides.
- **C-ANCA and P-ANCA levels** - Helpful if positive in diagnosis of Wegener granulomatosis and polyarteritis nodosa or microscopic polyangiitis, respectively.
- **Anti–glomerular basement membrane (anti-GBM) antibodies** - Highly suggestive of underlying Goodpasture syndrome.
- **Hepatitis B and C, HIV, Venereal Disease Research Laboratory (VDRL) serology** - Conditions associated with some glomerulonephritides.
Imaging Studies

Imaging studies help in assessing the damage in the physical structure of the kidneys. Some of the indicated imaging studies are:

- **Plain abdominal x-ray** - Particularly useful to look for radio-opaque stones or nephrocalcinosis.
- **Intravenous pyelogram** - Not commonly used because of potential for intravenous contrast renal toxicity; often used to diagnose renal stones.
- **Renal ultrasound** - Small echogenic kidneys are observed in advanced renal failure. Kidneys usually are normal in size in advanced diabetic nephropathy, where affected kidneys initially are enlarged from hyperfiltration. Structural abnormalities, such as polycystic kidneys, also may be observed. This is a useful test to screen for hydronephrosis, which may not be observed in early obstruction, or involvement of the retroperitoneum with fibrosis, tumor, or diffuse adenopathy. Retrograde pyelogram may be indicated if a high index of clinical suspicion for obstruction exists despite a negative study finding.
- **Renal radionuclide scan** - Useful to screen for renal artery stenosis when performed with captopril administration but is unreliable for GFR of less than 30 mL/min/1.73m²; also quantitates differential renal contribution to total GFR.
- **CT scan** - CT scan is useful to better define renal masses and cysts usually noted on ultrasound. Also, it is the most sensitive test for identifying renal stones. IV contrast-enhanced CT scans should be avoided in patients with renal impairment to avoid acute renal failure; this risk significantly increases in patients with moderate-to-severe CKD. Dehydration also markedly increases this risk.
- **MRI** is very useful in patients who require a CT scan but who cannot receive intravenous contrast. It is reliable in the diagnosis of renal vein thrombosis, as are CT scan and renal venography. Magnetic resonance angiography also is becoming more useful for diagnosis of renal artery stenosis, although renal arteriography remains the criterion standard.
- **Voiding cystourethrogram (VCUG)** - Criterion standard for diagnosis of vesicoureteral reflux.

References:

Can we prolong life of patients with advanced chronic kidney disease: what is the clinical evidence?
Stompór T, Olszewski A, Kierzkowska I.

Source
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Abstract
The risk of death in patients with advanced chronic kidney disease (CKD) is markedly higher than in the population without CKD, even in patients suffering from advanced cardiovascular disease. Among several clinical features of CKD, the following are considered the most important areas of therapeutic intervention: hypertension, lipid abnormalities, mineral and bone disorders of CKD (previously known as renal osteodystrophy), renal anemia, and uremic toxicity. However, numerous treatment strategies, which are applied based on the understanding of underlying pathologies, did not result in significantly improved prognosis. These strategies include lowering of blood pressure, use of statins, control of hyperphosphatemia and hyperparathyroidism, erythropoiesis-stimulating agents, use of better and more biocompatible dialysis membranes, and higher dialysis dose. In this critical review, we discuss the most important, large clinical trials, in which the above therapies failed to show desirable results and to reduce mortality in patients with advanced CKD.


Cardiovascular complications in CKD patients: Role of oxidative stress.
Gosmanova EO, Le NA.

Source
Nephrology Division, Department of Medicine, The University of Tennessee Health Science Center, Memphis, TN 38103, USA.

Abstract
Starting with the early stages, patients with chronic kidney disease (CKD) experience higher burden of cardiovascular disease (CVD). Moreover, CVD complications are the major cause of mortality in CKD patients as compared with complications from chronic kidney failure. While traditional CVD risk factors, including diabetes, hypertension, hyperlipidemia, obesity, physical inactivity, may be more prevalent among CKD patients, these factors seem to underestimate the accelerated cardiovascular disease in the CKD population. Search for additional biomarkers that could explain the increased CVD risk in individuals with CKD has gained increasing importance. Although it is unlikely that any single nontraditional risk factor would fully account for the increased CVD risk in individuals with CKD, oxidative stress appears to play a central role in the development and progression of CVD and its complications. We will review the data that support the contribution of oxidative stress in the pathogenesis of CVD in patients with chronic kidney failure.
Undiagnosed kidney disease in hospitalised patients: an opportunity for improvement.


Source
Internal Medicine Department, Hospital de Alcañiz, Teruel, Spain.

Abstract

OBJECTIVES:
In hospitalised patients, chronic kidney disease (CKD) is associated with a high risk of morbidity, mortality and drug toxicity. We identified care improvement opportunities in hospitalised patients with kidney disease in a regional hospital.

MATERIAL AND METHOD:
Clinical audit: 200 patients hospitalised for any reason in Alcañiz Hospital (Spain) were randomly selected. The data sources were laboratory data, clinical history and discharge reports. RIFLE criteria were applied to define kidney function deterioration. As process quality indicators we used: 1) percentage of hospitalised patients with at least one determination of kidney function during admission. 2) percentage of patients who met criteria for CKD and/or kidney function deterioration and who had this diagnosis recorded in clinical progress reports. 3) percentage of patients who met criteria for CKD and/or kidney function deterioration and who had this diagnosis recorded in the discharge report.

RESULTS:
Mean age was 71.1 (17) years, 42% women, 63% admitted to medical areas and 37% to surgical areas. Some 194 patients had a kidney function determination at admission; however during their stay kidney function was not monitored in 54 patients (27%), especially in surgical areas. CKD diagnosis by analyses prior to admission was available for 50 patients (25%); however this diagnosis figures in the clinical history in 14 of them (28%), and in the discharge report in 17 (34%). Kidney function deterioration was detected in 68 of the 146 patients who had kidney function monitoring during hospitalisation (46.5%). This information was contained in the clinical history in only 50% of cases and in the discharge report in 33.8%.

CONCLUSIONS:
The incidence of CKD prior to admission and deterioration of kidney function during hospitalisation are high. Often these diagnoses are not included in clinical progress reports or in the discharge report, reflecting poor condition awareness on the part of our colleagues. Implementation of a clinical protocol and its diffusion throughout the hospital may be important tools to achieving more efficient and consistent management of these conditions.
Quality of life in chronic kidney disease.
[Article in English, Spanish]

Abstract

BACKGROUND:
The evaluation of health-related quality of life (QOL) in chronic kidney disease intends to quantify its consequences, according to the patient’s subjective perception.

AIM:
To evaluate the health-related QOL in four groups of patients followed at our Nephrology Department: chronic kidney disease (CKD) stages 1-4, kidney transplant (KT), haemodialysis (HD) and peritoneal dialysis (PD) patients.

PATIENTS AND METHODS:
Thirty patients with CKD stages 1-4 and 30 KT patients were randomly selected. All patients from our Haemodialysis and Peritoneal Dialysis Units with capacity to answer the inquiry (37 and 14, respectively) were also selected. The instruments applied were the SF-36 and KDQOL-SF 1.3.

RESULTS:
The four groups presented better results in the Social Functioning scale (77.68 ± 18.46 in PD; 74.17 ± 29.53 in KT; 66.81 ± 31.39 in CKD 1-4; 62.16 ± 32.84 in HD; p = 0.192). The lowest results appeared in the General Health scale (39.92 ± 19.12 in CKD; 45.95 ± 21.56 in HD; 47.13 ± 23.15 in KT; 51.79 ± 18.89 in PD; p = 0.321). Peritoneal dialysis patients achieved the best results in the Physical Health Component, but this difference disappeared after adjustment to confounding factors. Age, gender and haemoglobin level were the variables related with QOL. However, PD patients obtained better scores comparing to HD patients in the following KDQOL-SF scales: Effects of kidney disease, Burden of kidney disease and Patient satisfaction (p <0.05).

CONCLUSIONS:
Health-related QOL was better in peritoneal dialysis patients comparing to haemodialysis patients in specific scales of chronic kidney disease. Age, gender and haemoglobin level interfered with health-related QOL.
**End-stage renal disease preceded by rapid declines in kidney function: a case series.**
Lee P, Johansen K, Hsu CY

**Source**
Division of Nephrology, University of California, San Francisco, San Francisco, CA, USA.

**Abstract**

**BACKGROUND:**
Few studies have defined alternate pathways by which chronic kidney disease (CKD) patients transition into end-stage renal disease (ESRD).

**METHODS:**
We studied all consecutive patients initiated on maintenance hemodialysis or peritoneal dialysis over several years at two dialysis units in Northern California. Rapid decline in kidney function was considered to have occurred if a patient was documented to have estimated GFR > 30 mL/min/1.73 m² within three months prior to the initiation of chronic dialysis.

**RESULTS:**
We found that 8 out of 105 incident chronic dialysis patients one dialysis unit (7.6%; 95% confidence interval 3.4-14.5%) and 9 out of 71 incident patients at another (12.7%, 95% CI 6.0%-22.7%) suffered rapid decline in kidney function that was the immediate precipitant for the need for permanent renal replacement therapy. All these patients started hemodialysis and all relied on catheters for vascular access. Documentation submitted to United States Renal Data System did not fully reflect the health status of these patients during their “pre-ESRD” period.

**CONCLUSIONS:**
A sizeable minority of ESRD cases are preceded by rapid declines in kidney function. The importance of these periods of rapid decline may have been under-appreciated in prior studies of the natural history of CKD and ESRD.

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**Assessing kidney function in Asia.**
Ho E, Teo BW.

**Source**
Department of Medicine, Yong Loo Lin School of Medicine, National University of Singapore, Singapore.

**Abstract**

An equation for accurate estimation of the glomerular filtration rate (GFR) is vital for staging and directing the treatment of chronic kidney disease (CKD), which is a source of considerable morbidity and mortality around the world. The Modification of Diet for Renal Disease (MDRD) equation, which includes a racial coefficient, is commonly used. The MDRD equation has been validated in Caucasian populations, but modifying the racial coefficient for Asian countries has resulted in substantially different values that may not be due to race alone. Moreover, it is sometimes difficult to define race, particularly in multi-ethnic populations and among offspring of inter-ethnic marriages. Furthermore, the precision of the MDRD equation is poorer at the early stages of CKD. New markers, such as cystatin C, and new equations may be needed to accurately assess wider ranges of GFR in multi-ethnic countries. We review the development of GFR-estimating equations from an Asian perspective.
Cardiorenal syndromes: pathophysiology to prevention.
McCullough PA.

Abstract
There is a strong association between both acute and chronic dysfunction of the heart and kidneys with respect to morbidity and mortality. The complex interrelationships of longitudinal changes in both organ systems have been difficult to describe and fully understand due to a lack of categorization of the common clinical scenarios where these phenomena are encountered. Thus, cardiorenal syndromes (CRSs) have been subdivided into five syndromes which represent clinical vignettes in which both the heart and the kidney are involved in bidirectional injury and dysfunction via a final common pathway of cell-to-cell death and accelerated apoptosis mediated by oxidative stress. Types 1 and 2 involve acute and chronic cardiovascular disease (CVD) scenarios leading to acute kidney injury (AKI) or accelerated chronic kidney disease (CKD). Types 3 and 4 describe AKI and CKD, respectively, leading primarily to heart failure, although it is possible that acute coronary syndromes, stroke, and arrhythmias could be CVD outcomes in these forms of CRS. Finally, CRSs type 5 describe a systemic insult to both heart and the kidneys, such as sepsis, where both organs are injured simultaneously in persons with previously normal heart and kidney function at baseline. Both blood and urine biomarkers, including the assessment of catalytic iron, a critical element to the generation of oxygen-free radicals and oxidative stress, are reviewed in this paper.

Prediction of ESRD and death among people with CKD: the Chronic Renal Impairment in Birmingham (CRIB) prospective cohort study.

Abstract
BACKGROUND: Validated prediction scores are required to assess the risks of end-stage renal disease (ESRD) and death in individuals with chronic kidney disease (CKD).

STUDY DESIGN: Prospective cohort study with validation in a separate cohort.

SETTING & PARTICIPANTS: Cox regression was used to assess the relevance of baseline characteristics to risk of ESRD (mean follow-up, 4.1 years) and death (mean follow-up, 6.0 years) in 382 patients with stages 3-5 CKD not initially on dialysis therapy in the Chronic Renal Impairment in Birmingham (CRIB) Study. Resultant risk prediction equations were tested in a separate cohort of 213 patients with CKD (the East Kent cohort). FACTORS: 44 baseline characteristics (including 30 blood and urine assays).

RESULTS: In the CRIB cohort, 190 patients reached ESRD (12.1%/y) and 150 died (6.5%/y). Each 30% lower baseline estimated glomerular filtration rate was associated with a 3-fold higher ESRD rate and a 1.3-fold higher death rate. After adjustment for each other, only baseline
After adjustment for each other, only baseline creatinine level, serum phosphate level, urinary albumin-creatinine ratio, and female sex remained strongly (P < 0.01) predictive of ESRD. For death, age, N-terminal pro-brain natriuretic peptide, troponin T level, and cigarette smoking remained strongly predictive of risk. Using these factors to predict outcomes in the East Kent cohort yielded an area under the receiver operating characteristic curve (ie, C statistic) of 0.91 (95% CI, 0.87-0.96) for ESRD and 0.82 (95% CI, 0.75-0.89) for death.

LIMITATIONS:
Other important factors may have been missed because of limited study power.

CONCLUSIONS:
Simple laboratory measures of kidney and cardiac function plus age, sex, and smoking history can be used to help identify patients with CKD at highest risk of ESRD and death. Larger cohort studies are required to further validate these results.


Drug therapy in patients with chronic renal failure.
Hartmann B, Czock D, Keller F.

Source
Universität Ulm, Medizinische Fakultät, Nephrologie, Ulm, Germany.

Abstract

BACKGROUND:
Roughly 20% of patients in hospital have impaired kidney function. This is frequently overlooked because of the creatinine-blind range in which early stages of renal failure are often hidden. Chronic kidney disease is divided into 5 stages (CKD 1 to 5).

METHODS:
Selective literature search.

RESULTS:
Methotrexate, enoxaparin and metformin are examples of drugs that should no longer be prescribed if the glomerular filtration rate (GFR) is 60 mL/min or less. With antidiabetic (e.g. glibenclamide), cardiovascular (e.g. atenolol) or anticonvulsive (e.g. gabapentin) drugs, the advice is to use alternative preparations such as gliquidone, metoprolol or carbamazepine which are independent of kidney function. Drug dose adjustment should be considered with antimicrobial (e.g. ampicillin, cefazolin), antiviral (e.g. aciclovir, oseltamivir) and, most recently, also for half of all chemotherapeutic and cytotoxic drugs in patients with impaired kidney function (with e.g. cisplatin, for instance, but not with paclitaxel).

CONCLUSION:
Decisions concerning drug dose adjustment must be based on the pharmacokinetics but this is an adequate prerequisite only in conjunction with the pharmacodynamics. There are two different dose adjustment rules: proportional dose reduction according to Luzius Dettli, and the half dosage rule according to Calvin Kunin. The latter leads to higher trough concentrations but is probably more efficient for anti-infective therapy.
Possible Link between Metabolic Syndrome and Chronic Kidney Disease in the Development of Cardiovascular Disease.
Nitta K

Source
Department of Medicine, Kidney Center, Tokyo Women's Medical University, 8-1 Kawada-cho, Shinjuku-ku, Tokyo 162-8666, Japan.

Abstract
Metabolic syndrome (MetS) is a clinical syndrome that consists of visceral obesity, dyslipidemia, hypertension, and impaired insulin sensitivity. Although individual components of MetS have been implicated in the development of chronic kidney disease (CKD), few studies have examined the effect of combinations of the components of MetS on the development of CKD and cardiovascular disease (CVD). The prevalence of MetS is increasing worldwide in both developing and developed countries, and early detection and treatment of MetS would be a cost-effective strategy for preventing the development of CKD. Visceral obesity and insulin resistance are two important features of MetS that may be associated with renal damage. Lifestyle modifications, including caloric restriction and exercise, are necessary to treat MetS. Initial antihypertensive therapy should consist of an angiotensin-converting enzyme inhibitor or angiotensin receptor blocker. An improved understanding of the mechanism responsible for the association between MetS and renal damage should be helpful in determining the treatment regimens directed at cardiovascular and renal protection.