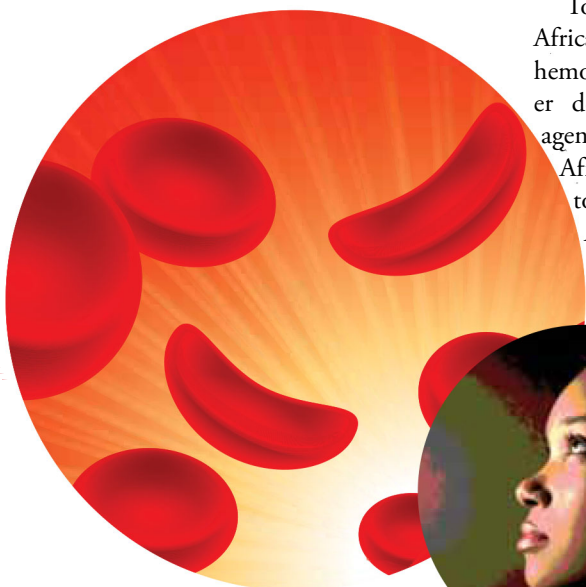


Kidney News

March 2014 | Vol. 6, Number 3

Sickle Cell Trait in African Americans Undergoing Dialysis Patients May Affect ESA Dosing



To reach the same level of hemoglobin, African American dialysis patients with hemoglobinopathy traits required higher doses of erythropoiesis-stimulating agents (ESAs) during dialysis than other African American patients, according to a *Journal of the American Society of Nephrology* study.

“This research is important because it is the largest study to evaluate how sickle cell trait affects anemia treatment in African American hemodialysis patients,” said first author Vimal Derebail, MD, MPH, of the University of North Carolina at Chapel Hill and the UNC Kidney Center.

Sickle cell study results

Sickle cell trait represents the carrier state of sickle cell disease and is present in an estimated 6 percent to 8 percent of African Americans. While sickle cell disease

is characterized by abnormally shaped red blood cells that can block blood flow and cause organ damage, the carrier state—called sickle cell trait—is generally thought to be benign. Kidney abnormalities have been reported in some individuals with sickle cell trait, however.

Derebail and his team wondered whether the presence of sickle cell trait among African Americans might impact ESA dosing in those on dialysis, many of whom require higher doses than their Caucasian counterparts. Previous research had shown that uremic toxins alter erythrocytes. Transit through a hemodialysis circuit could predispose to sickling of red blood cells containing sickle cell trait as a result of exposure to lower temperature, lower partial pressure of oxygen, and physical stressors of the hemodialysis filter. Transient sickling events in erythrocytes may lead to a reduced life span of the cells.

In a cross-sectional, observational study, Derebail and his colleagues examined laboratory and clinical data over 6

Continued on page 2

The presence of traits for hemoglobinopathy such as that for sickle cell disease may help explain the need for greater doses of anemia medications administered to African Americans undergoing dialysis compared with Caucasians.



Inside

Journal View

Kids' growth improves posttransplant with steroid-free care

World Kidney Day

shines light on aging and kidney disease

Detective Nephron

What is causing a young woman's hematuria and increase in creatinine?

Policy Update

SGR fix continues to elude Congress

Kidney Health Initiative

announces 60 pioneer members

Pediatric CKD Progression Model Identifies Children at Highest Risk for ESRD

By Kurtis Pivert

A new model could predict which children with chronic kidney disease (CKD) are at highest risk for progressing to end stage renal disease (ESRD) well before they lose renal function. Using existing patient

data, the composite scoring system would facilitate early intervention, giving nephrologists the opportunity to slow the disease course. The model, recently published in the *Clinical Journal of the American Society of Nephrology*, is

the first specifically designed to assess the unique characteristics of children with CKD (1). Although further validation in a larger population is needed, the system could be a valuable resource for the pediatric kidney care team.

“Clinicians could easily apply this tool in their practice, since our model uses routinely available clinical and laboratory data, and can predict the long-term risk for renal impairment with accuracy,” said senior author Ed-

Continued on page 3



Sickle Cell Trait

Continued from page 1

months in 2011 for 5319 adult African American hemodialysis patients, 542 (10.2 percent) of whom had sickle cell trait and 129 (2.4 percent) of whom had hemoglobin C trait. A total of 5002 patients (10.3 percent sickle cell trait and 2.4 percent hemoglobin C trait) received ESAs. (In people with hemoglobin C trait, some of the hemoglobin in the blood is an abnormal form, called hemoglobin C. People with hemoglobin C disease have mostly hemoglobin C, which can reduce the number and size of red blood cells in the body, causing mild anemia.)

The researchers found that patients with hemoglobinopathy traits received higher median doses of ESA than patients with normal hemoglobin (4737.4 vs. 4364.1 units/treatment). Hemoglobinopathy traits were linked with 13.2 percent more ESAs per treatment to achieve nearly identical hemoglobin even after controlling for known potential confounding factors. Within subgroups, sickle cell trait patients received 13.2 percent more ESAs per treatment, and hemoglobin C trait patients received 12.9 percent more. Patients with either hemoglobinopathy had a 30 percent increase in the likelihood of falling

in the highest quartile of ESA dosing.

“Although individuals with sickle cell trait do not manifest typical vaso-occlusive symptoms, as observed in patients with sickle cell disease, this study by Derbail and colleagues provides further evidence that sickle cell trait may not be as benign as previously thought,” said Kenneth Ataga, MD, who was not involved with the study and is the director of the UNC Comprehensive Sickle Cell Program. “While it is reasonable to postulate that this increased ESA requirement is related to the presence of sickle hemoglobin, this does not provide an explanation for those individuals with hemoglobin C trait, who do not have sickle hemoglobin.”

The study also found that sickle cell trait was slightly more common among dialysis patients, present in 10 percent of study participants compared with 6.5 percent to 8.7 percent in the general African American population.

Bundled payment adjusts for sickle cell disease, but not trait

By connecting sickle cell trait with increased ESA use in African Americans undergoing dialysis, the findings may have important policy implications.

Presently, Medicare bundled payments

for dialysis allow adjustment for several chronic diseases including sickle cell disease, but not sickle cell trait, which is far more common than sickle cell disease and other potential modifiers of anemia,” Derbail said. “While we don’t know whether there are any adverse consequences to this higher dose of medication yet, further policies and decisions regarding management of anemia in dialysis patients should take into account these findings.”

The researchers calculated that with the average wholesale price of ESA at \$1,518 per 100 units, and the average ESA dose being 6100 units per treatment in patients with normal hemoglobin, these traits would account for a \$12.10 increase in cost of each dialysis treatment. Conservatively estimating an average of 140 treatments yearly, this increase amounts to an incremental expense of more than \$1 million annually in the study cohort. When the findings are extrapolated to the U.S. hemodialysis population of more than 140,000 African Americans who fall within the group of 7 percent to 14 percent with hemoglobinopathy traits, the cost of ESAs attributable to these traits is between \$16.8 and \$33.5 million per year.

“In addition to considering the cost implications of this increased ESA requirement, more studies are required to ascer-

tain the mechanism for increased ESA requirement in sickle cell trait as well as hemoglobin C trait,” Ataga said.

Because the study also revealed that sickle cell trait is somewhat more common in the dialysis population than in the general population, it raises the question of whether sickle trait might contribute to kidney disease. Additional studies are needed to test this possibility, the researchers said. ●

Study co-authors include Eduardo Lacson, Jr., MD, Abhijit Kshirsagar, MD, Nigel Key, MB ChB, Susan Hogan, PhD, Raymond Hakim, MD, Ann Mooney, MSN, Chinu Jani, SC, Curtis Johnson, Yichun Hu, MS, Ronald Falk, MD, and J. Michael Lazarus, MD.

Disclosures: Drs. Lacson, Hakim, and Lazarus and Ms. Mooney were employed by FMCNA, the sponsor, at the time of the study. Mr. Johnson and Mr. Jani are employed by Spectra Laboratories, Inc.

The article, entitled “Sickle Trait in African American Hemodialysis Patients and Higher Erythropoiesis-Stimulating Agent Dose,” is available online at <http://jasn.asnjournals.org/>, doi: 10.1681/ASN.2013060575.

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Pediatric CKD Progression Model

Continued from page 1

uardo Oliveira, PhD. “The variables included in our model have been considered in many studies of risk factors in adult and pediatric patients.”

Oliveira and his coworkers from the Federal University of Minas Gerais in Brazil developed the predictive score using 18 years’ worth of data from their pediatric CKD clinic. Information obtained from 147 children with CKD who received treatment in the clinic’s multidisciplinary setting (comprising pediatric nephrologists, as well as pediatricians, nurses, nutritionists, and social workers) was included in their analysis.

Primary renal disease, ethnicity, age, baseline eGFR, proteinuria, and uncontrolled hypertension were among the numerous patient characteristics assessed in the scale’s development. Progression to stage 5 CKD was designated as a dependent variable, and renal survival defined as the date of dialysis initiation or first eGFR level of less than 15 mL/min/1.73 m².

After multivariate analysis, three criteria were found to be independent predictors of children progressing to ESRD: baseline eGFR, proteinuria (dichotomized as either severe or absent/mild), and primary renal disease (dichotomized as glomerulonephritis or other renal diseases). Each of the three variables were weighted to construct a 13-point predictive score stratifying patients into low-, medium-, and high-risk groups for developing renal failure (Table 1). The score was tested against long-term follow-up data from their patient cohort (median follow-up 53 months) to determine how closely the forecasted risk matched the observed results.

At both 2 and 5 years of follow-up, the model closely predicted the observed outcome for all three risk groups. However, more deviation was demonstrated at the 10- and 15-year follow-up points. Oliveira cautioned that “as we pointed out in our paper, it is clear that our model needs to be validated in a large prospective cohort.”

Children are not small adults

“Proteinuria and etiology are key variables in the adult CKD population, and now this has been validated in children, providing a scientific basis for practice,” said Deepa Chand, MD, FASN, chief of pediatric nephrology at Rush University Medical Center in Chicago, IL. “Intuitively, etiologies that have higher proteinuric states are more deleterious and this study provides the data supporting this theory. It is important to note that, unlike adult CKD patients, protein intake is not restricted in pediatric CKD patients but rather optimized so as to prevent protein malnutrition.” Chand

added that the inclusion of baseline eGFR in the scale was a curious finding, but that it stresses the need for early referral to a pediatric nephrologist.

Until now, there have been no CKD to ESRD progression models for the pediatric CKD setting. This is due in part to the difficulty in performing pediatric CKD studies given the relatively small volume of patients, said Chand, who was not affiliated with the study. Both pediatric and adult CKD populations share similar characteristics, she noted. Medication adherence in both groups can be challenging and contribute to the rate of renal function progression. However, the etiologies of pediatric CKD differ from those of adults.

“Because anatomic abnormalities are more prevalent, proteinuria is often a later finding in children, which, as the authors have identified, plays a key role in disease progression,” Chand said.

Unlike adults with CKD, children with kidney disease are also undergoing somatic growth and neurocognitive development, which can complicate the process of predicting progression.

“Times of maximal growth velocity can precipitate decline in renal function in children, as the metabolic demands cannot be accommodated by the dysfunctional kidneys,” said Chand. “Somatic growth in children with CKD is often altered because they do not follow typical growth curves. Acidosis, more prevalent in pediatric patients because of the tubular acidification defect from congenital renal disease, alters growth hormone secretion and contributes to growth retardation. Altered taste sensation is also common in children with CKD, making adequate nutritional intake difficult.”

Preventing neurocognitive delays is a major goal in children with CKD and a key difference in the management of pediatric versus adult CKD patients, Chand emphasized. “A variety of factors, including acidosis, anemia, and uremia, contribute to this delay. It is imperative that these patients receive appropriate therapy services, such as physical, occupational, and speech to ameliorate these effects,” she said.

Individualizing the approach to slow progression

Using the predictive model to stratify patient risk for renal failure can “assist professionals involved in the care of these patients, who may possibly establish appropriate measures for each risk group,” Oliveira said. He noted this could include more intensive preventive measures for those identified as being at high risk for progression to ESRD.

Chand underscored that the multidisciplinary approach used by Oliveira was also key for identifying progres-



Table 1: Pediatric CKD Predictive Scoring Model

Category	Variable	Score
Proteinuria	severe	5
	absent/mild	0
Etiology	glomerulonephritis	3
	other	0
baseline eGFR (mL/min/1.73 m ²)	>70	0
	59–69.9	1
	48–58.9	2
	37–47.9	3
	26–36.9	4
	15–25.9	5
total possible score		13
Risk for Progression to ESRD		
low risk		0–4
medium risk		5–7
high risk		8–13
CKD = chronic kidney disease. eGFR = estimated glomerular filtration rate. ESRD = end stage renal disease.		

sion and early intervention in children with kidney disease.

“The authors provide an excellent predictive model of CKD progression. Pediatric nephrology practices can optimize use of the multidisciplinary approach, with maximized education and monitoring of eGFR, proteinuria, and growth,” Chand said. “As with the adult CKD population, progression of proteinuria is a significant contributor to rate of kidney function decline. The authors have highlighted proteinuria and hypertension management as targets for the practitioner. This is critical if prevention of progression is possible.”

Although the predictive model can assist in identification of children at risk, early referral to pediatric nephrologists is vital to improving outcomes in this population. “This is an important point for our general pediatrician colleagues and could prove to be a very valuable concept in the management of these children,” Chand said. ●

Reference

1. Cerqueira DC, et al. A predictive model of progression of CKD to ESRD in a predialysis pediatric interdisciplinary program. *Clin J Am Soc Nephrol*. doi: 10.2216/CJN.06630613.



KidneyNews

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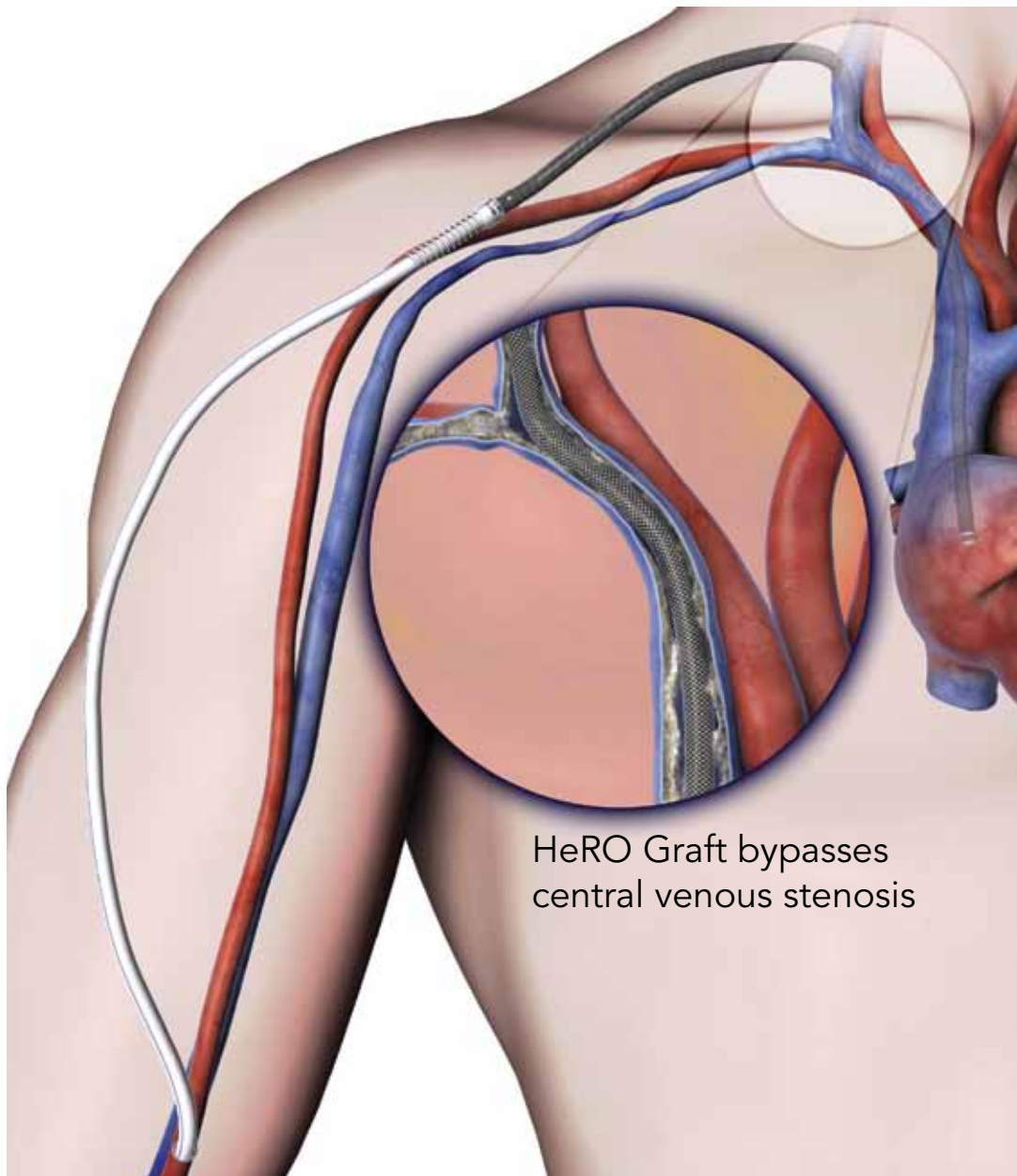
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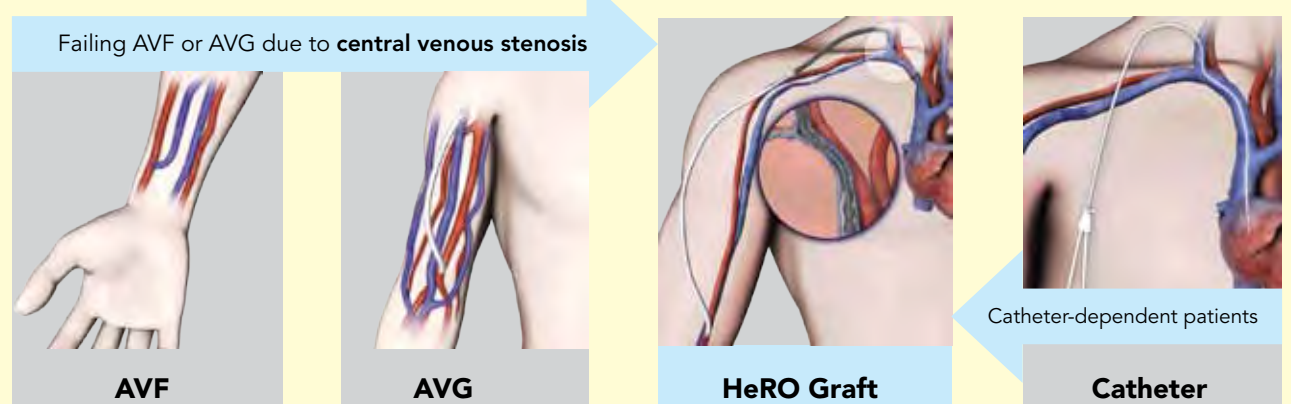
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1) Katzman et al., J Vasc Surg 2009. 2) Gage et al., EJVES 2012. 3) Dageforde et al., JSR 2012.

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Journal View

When Is Renal Artery Revascularization Beneficial?

Flash pulmonary edema is a high-risk indication for renal artery revascularization, but declining kidney function and refractory hypertension may not be, reports a study in the *American Journal of Kidney Diseases*.

The researchers analyzed one hospital's experience of 467 patients with renal artery stenosis of 50 percent or greater,

treated according to clinical presentation and physician and patient preference. Flash pulmonary edema was present in 7.8 percent of patients, refractory hypertension in 24.3 percent, and rapidly declining kidney function in 9.7 percent. Treatment and outcomes were compared for patients with versus without these high-risk characteristics.

Renal artery revascularization was performed in 32 percent of patients with flash pulmonary edema, 28 percent with rapidly declining kidney function, and 28 percent with refractory hypertension. At a median 3.8 years of follow-up, 55 percent of patients had died, 33 percent had a cardiovascular (CV) event, and 18 percent had ESRD.

In patients treated medically, flash pulmonary edema was associated with an increased risk of death and CV events: hazard ratio 2.2 and 3.1, respectively. Rapidly declining kidney function and refractory hypertension were not associated with increased risk of adverse outcomes. Among patients with flash pulmonary edema, the risk of death was lower for those undergoing revascularization (HR 0.4) in comparison with medical management, but there was no difference in CV events or ESRD.

Revascularization did not reduce adverse outcomes in patients with rapidly declining kidney function or refractory hypertension. For the 31 patients who had both of these high-risk characteristics, revascularization was associated with a reduced risk of death (HR 0.15) and CV events (HR 0.23).

Recent studies have questioned the use of revascularization for patients with renovascular atherosclerosis and stable kidney disease. However, these findings may not apply to patients with high-risk presentations.

The new study suggests that revascularization is indicated for patients with flash pulmonary edema, consistent with current guidelines. More research is needed to determine the benefit of revascularization for patients with rapidly declining kidney function plus refractory hypertension [Ritchie J, et al. High-risk clinical presentations in atherosclerotic renovascular disease: prognosis and response to renal artery revascularization. *Am J Kidney Dis* 2014; 63:186–197]. ●

One-Time FGF23 Level Predicts Cardiovascular Risk in CKD

A single measurement of fibroblast growth factor-23 (FGF23) predicts the risk of cardiovascular events in patients with chronic kidney disease (CKD), reports *Nephrology Dialysis Transplantation*.

The study included 439 adults with CKD whose median estimated GFR was 36 mL/min per 1.73 m², drawn from a larger randomized trial. All had paired samples for measurement of FGF23 over 2 years. Changes in FGF23 and time-averaged FGF23 were compared with one-time values as predictors of clinical events.

Both one-time and time-averaged FGF23 were positively associated with a primary composite outcome of myocardial infarction, stroke, and cardiovascular mortality. There were also significant associations for overall mortality, start of renal replacement therapy, and congestive heart failure.

One-time and time-averaged FGF23 had similar predictive value: adjusted hazard ratio 1.71 and 1.91 for the composite outcome, respectively. Change in FGF23



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over time was associated only with the start of renal replacement therapy. The median FGF23 value increased from 109 to 149 U/mL over 2 years.

Fibroblast growth factor-23 increases with progression of CKD and is an independent predictor of adverse clinical events. This prospective study confirms that FGF23 is a cardiovascular risk factor in CKD, and it shows that two measurements do not improve the predictive value over a one-time FGF23 value. The authors note that their study included relatively short follow-up times and did not specifically target FGF23 levels [Bouma-de Krijger A, et al. Time-averaged level of fibroblast growth factor-23 and clinical events in chronic kidney disease. *Nephrol Dial Transplant* 2014; 29:88–97]. ●

Worldwide Increase in Mortality Soon After Start of Dialysis

Data from many different countries show that the first few months after the start of dialysis are a high-risk period for mortality, reports a study in *Kidney International*.

The researchers analyzed data on nearly 87,000 patients from 11 countries, submitted to the Dialysis Outcomes and Practice Patterns Study (DOPPS). All-cause mortality in the early period within 120 days after the start of dialysis was compared with the intermediate period (121 through 365 days) and late period (after 365 days). Analyses were adjusted for age, sex, race, and presence of diabetes.

The rate of death per 100 patient-years was 26.7 during the early period after the start of dialysis, decreasing to 16.9 in the intermediate period and 13.7 in the late period. All 11 countries had higher mortality in the early period than in the intermediate period. Adjusted hazard ratios (HRs) for the early period versus the intermediate period varied considerably: 3.1 in Japan; 1.6 to 1.8 in Australia/New Zealand, Belgium, and Italy; 1.3 to 1.5 in Canada, France, Germany, Sweden, and the United States; and 1.2 in the United Kingdom. For the late period versus the intermediate period, the HRs were closer to 1.

The risk of death during the early period was higher for older patients than for younger patients (HR 1.59 versus 1.08), for female patients than for male patients (HR 1.62 versus 1.46), and for patients without diabetes as the primary cause of ESRD (HR 1.62 versus 1.39). During all periods, most countries had lower mortality than did the United States.

Previous studies have reported increased mortality early after the beginning of dialysis. This study suggests a higher risk of death during the first 120 days in patients receiving dialysis in all

countries participating in the DOPPS. Early mortality differs between countries; the United States is on the higher end of the range. The investigators conclude, “Efforts to improve outcomes should focus on the transition period and the first few months of dialysis” [Robinson BM, et al. Worldwide, mortality risk is high soon after initiation of hemodialysis. *Kidney Int* 2014; 85:158–165]. ●

Good Growth after Steroid-Free Transplantation in Kids

For children undergoing kidney transplantation, steroid-free immunosuppression is safe and reduces the long-term risks of obesity and short stature, reports a study in *Pediatric Transplantation*.

The researchers report on the outcomes of a strategy of complete steroid

avoidance after pediatric renal transplantation. The analysis included 65 transplants in 60 patients performed in one Danish hospital from 1994 through 2009. Most patients received antithymocyte globulin for induction;

Continued on page 9

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Journal View

Good Growth

Continued from page 7

for immunosuppression they received a calcineurin inhibitor and mycophenolate mofetil. The only indications for steroids were rejection or comorbid conditions.

Sixty percent of patients were male; the mean age at transplantation was 9.5 years. Mortality was 7 percent. Graft survival was 81 percent after 5 years and 63 percent after 10 years. There was a 9 percent rate of acute rejection within the first year after transplantation. Twenty-nine percent of children received steroids at some point during follow-up, most commonly for acute clinical rejection.

The children had a normal distribution of body mass index (BMI) before transplantation. Their mean pretransplantation BMI standard deviation score (SDS) of 0.21 remained stable over the subsequent 5 years. Growth improved significantly after transplantation; the mean height SDS increased from -1.7 to -1.1. Children younger than 6 years had the greatest catch-up growth; their height SDS increased from -2.1 to -0.9.

Alternative strategies have been developed to avoid the side effects of steroids in children undergoing organ transplantation. Steroid-free immunosuppression has shown good results in terms of graft function and rejection rates in children receiving kidney transplants.

This long-term follow-up shows that steroid-free transplantation not only is medically safe but also improves growth while controlling the development of obesity. Catch-up growth is particularly favorable in the youngest transplant recipients [Wittenhagen P, et al. Long-term experience of steroid-free pediatric renal transplantation: effects on graft function, body mass index, and longitudinal growth. *Pediatr Transplant* 2014; 18:35–41]. ●

Treatments to Prevent ESRD Are Less Effective in the “Real World”

In a real-world population of older adults at risk, interventions to prevent ESRD have a smaller effect size than reported in clinical trials, reports a study in *JAMA Internal Medicine*.

The simulation study used a retrospective cohort of more than 370,000 Department of Veterans Affairs (VA) patients with chronic kidney disease. Data from four major trials of angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers (ACEIs/ARBs) for prevention of ESRD were applied to this real-world, high-risk population. In the trials, with

follow-up times of 2.6 to 3.4 years, patients taking ACEIs/ARBs had relative risk reductions of 23 to 56 percent for ESRD.

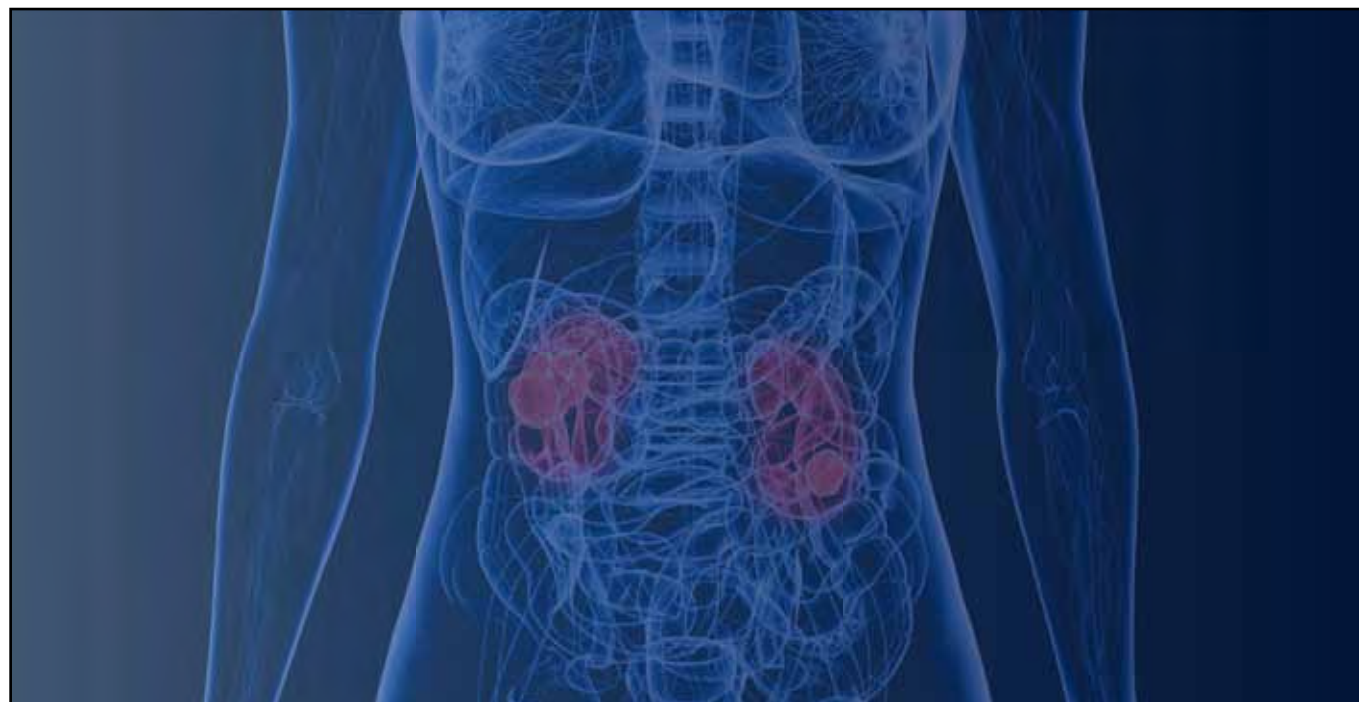
The reported numbers needed to treat (NNT) ranged from nine to 25. The researchers analyzed the expected impact of a 30 percent relative risk reduction on the NNT to prevent one case of ESRD over 3 years.

In the real-world VA population, the estimated NNT values varied widely according to the patients' baseline ESRD risk. For patients at highest risk (estimated GFR [eGFR] 15 to 29 mL/min per 1.73 m² and dipstick proteinuria 2+ or greater), NNT was 16. In contrast, for those at lowest risk (eGFR 45 to 59 mL per min/1.73 m² and negative or trace proteinuria, or eGFR 60 mL/min

per 1.73 m² or higher with 1+ proteinuria), the NNT to prevent one case of ESRD rose to 2500.

More than 90 percent of patients in the VA cohort fell into a group with an NNT of 100 or higher. The results were similar on sensitivity analysis and with up to 10 years of ACEI/ARB treatment. This was so in all sensitivity analyses

Continued on page 10



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Journal View

Treatments to Prevent ESRD

Continued from page 9

and with exposure time of up to 10 years.

All four clinical trials of ACEI/ARBs excluded patients older than age 70, with varying eligibility requirements related to diabetes and proteinuria. The new simulation study suggests that the effect size of ACEI/ARB treatment for preventing ESRD is likely to be substantially smaller in a real-world population of older patients with renal insufficiency, compared with the trial results. The investigators conclude, “This study highlights the importance of interpreting treatment effects from randomized clinical trials in the context of risk information from real-world clinical settings” [O’Hare AM, et al. Interpreting treatment effects from clinical trials in the context of real-world risk information: end-stage renal disease prevention in older adults. *JAMA Intern Med.* Published online January 13, 2014. doi:10.1001/jamainternmed.2013.13328]. ●

No “Obesity Paradox” in Type 2 Diabetes

In contrast to some previous reports, higher body mass index (BMI) is associated with increased mortality among patients with type 2 diabetes, concludes a study in the *New England Journal of Medicine*.

The researchers analyzed prospective follow-up data from 8970 women and 2457 men with type 2 diabetes, drawn from the Nurses’ Health Study and the Health Professionals Follow-up Study, prospectively. When the cohort members received diagnoses of diabetes, all were free of known cardiovascular disease and cancer. Prediagnosis BMI was analyzed as a predictor of long-term mortality. The analysis included 3083 deaths over an average follow-up time of 15.8 years.

Among all individuals with type 2 diabetes, there was a J-shaped association between all-cause mortality and BMI. Hazard ratio (HR) for death was 1.29 at a BMI of 18.5 to 22.4, compared with the reference category of 22.5 to 24.9. The HR then increased to 1.12 at a BMI of 25.0 to 27.4, 1.09 at 27.5 to 29.9, 1.24 at 30.0 to 34.9, and 1.33 at 35.0 or higher.

Among never-smokers, the HRs for all-cause mortality increased in linear fashion with BMI: HR 1.12 at a BMI of 18.5 to 22.4, 1.16 at 25.0 to 27.4, 1.21 at 27.5 to 29.9, 1.36 at 30.0 to

34.9, and 1.56 at 35.0 or higher. For individuals who had ever smoked, the association was nonlinear: HR 1.32, 1.09, 1.04, 1.14, and 1.21, respectively. Mortality increased in linear fashion for individuals younger than 65 years at diagnosis of diabetes but not for those who received their diagnoses at 65 or older.

Some studies have reported an ap-

parent “obesity paradox” in type 2 diabetes, with lower mortality among obese or overweight patients compared with those of normal weight. These prospective cohort data show a J-shaped association between BMI and mortality, overall and for patients with any history of smoking. For those who have never smoked, the risk of death increases in direct linear fashion with

BMI. “We did not observe a benefit of excess adiposity with regard to the risk of death,” the researchers write; “thus, our findings support the current recommendation that patients with diabetes achieve or maintain a normal weight” [Tobias DK, et al. Body-mass index and mortality among adults with incident type 2 diabetes. *N Engl J Med* 2014; 370:233–244]. ●

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Policy Update

Kicking the SGR Can Down the Road

By Mark Lukaszewski

Once again, Congress must address the sustainable growth rate (SGR) formula. The current law mandates an approximately 24 percent reduction to Medicare physician reimbursement for 2014. Each year Congress has prevented most of these pay cuts from taking effect. Although Congress has long recognized SGR's flaws, it has been unable to fund a permanent fix.

The SGR and the Congressional Budget Office

For every bill that costs money to implement, the Congressional Budget Office (CBO) issues a report estimating its cost over a 10-year period. Based on economic projections and other factors, this cost estimate is known as the bill's "score."

In February 2013, the CBO released a new report stating the cost of repealing the SGR system had been overestimated by nearly a billion dollars. It became apparent that it would cost more to fix the SGR than it would to abandon it and start from scratch. Clearly, the CBO understands the financial advantage of a new system.

So is Congress the problem?

If the CBO recognizes the benefits of replacing the SGR, it would be natural to assume the usual health care political games and congressional hold-ups that we have seen in the past are responsible for holding it up. But that assumption would be

wrong. Legislation to replace SGR is gaining tremendous bipartisan support in both the House and the Senate. So if there is agreement on both sides of the aisle that the SGR needs to go and consensus on the legislation that will get that accomplished why have negotiations not made any real significant progress in the past year on the \$150 billion bill? Where is the problem?

What is the Sustainable Growth Rate?

Implemented by Congress in 1997, the sustainable growth rate (SGR) attempts to control Medicare spending on physician fees by tying reimbursement to economic growth. If Medicare expenditures exceed the target set by the SGR, the formula calls for automatic reductions in physician payments.

The answer is the up-front cost of replacing the SGR. Offsets are needed to defray the cost of permanently replacing the SGR. In order for a replacement to be put into place, Congress has to either

cut money from other programs or come up with a new funding source. With such a large offset needed and few ideas for ways to pay for it, it looks like SGR will be receiving another Doc-Fix Act or "temporary patch."

Kicking SGR down the road?

Rather than fixing the problem with a new system, ASN expects Congress to mitigate the current symptom by passing a short-term patch, skirting the issue for the next 9 months. The short-term patch is estimated to cost approximately \$10 billion to \$15 billion and would cover the remainder of 2014. This patch would push SGR into a lame-duck session of Congress (the last 2 years of a president's second term in office). Lame-duck sessions tend to be less politically charged and could provide a more likely environment in which to attempt a permanent SGR replacement.

Although there are serious efforts in Congress to pass a permanent replacement for the SGR, it seems unlikely that such a solution will be realized anytime soon.

ASN strongly supports efforts to replace the SGR with a more stable system that accurately reflects the value of physicians' care, and is closely monitoring this issue on Capitol Hill. Stay tuned to *ASN Kidney News* as well as email communications from ASN to learn how you can get involved in advocating for a replacement to SGR. ●

World Kidney Day 2014 Highlights CKD and Aging

By Mark Lukaszewski and Grant Olan

Mark your calendars for World Kidney Day on March 13, 2014. Celebrated on the second Thursday of March every year, World Kidney Day is a joint initiative of the International Society of Nephrology (ISN) and International Federation of Kidney Foundations (IFKF) to raise awareness about kidney disease. World Kidney Day started in 2006 and highlights a different theme every year. This year's theme is "Chronic Kidney Disease (CKD) and Aging."

The older adult population is rapidly growing. More than 40 million Americans are over 65 today compared to 25 million in 1980. Furthermore, nearly half of those who are 70 or older have kidney disease. Patients with CKD usually require complicated medication routines, difficult dietary restrictions, and frequent medical visits. They are also more likely to have multiple comorbidities such as cardiovascular disease and diabetes. As age and disease progress, frailty becomes an issue.

All of these issues combine to make the care of older adults much more difficult than the care of younger patients, which is why ASN is commem-

orating World Kidney Day by releasing a suite of informational resources to increase understanding about kidney health in older adults and managing their care.

The ASN CKD Advisory Group developed a video for primary care physicians that reviews these issues. The video features CKD Advisory Group Member Deidra C. Crews, MD, FASN, and Alicia I. Arbaje, MD, from Johns Hopkins University addressing a number of topics, including screenings, interpretation of lab reports, specialist referrals, drug safety issues, monitoring treatment, and helping patients and families manage complex medical regimens.

The ASN Geriatric Nephrology Advisory Group also developed information for older adults to help them understand kidney disease and their care options. This information, slated for national release through a number of media outlets, will help older adults learn what kidney disease is, how a kidney disease diagnosis might impact their lives, and help guide them toward the right questions to ask about maintaining kidney health and options in the event of kidney failure.



Recognizing the importance of this issue, the Geriatric Nephrology Advisory Group recently updated a complementary online curriculum for providers that is currently available on the ASN website at www.asn-online.org. The Geriatric Nephrology Advisory Group also released a complementary video series for providers in 2012 that focuses on improving dialysis rounds for older adults. The curriculum and videos—available at www.asnrounds.org—are part of ASN's continued efforts to promote the highest quality care for patients, including older adults. ●



KIDNEY HEALTH INITIATIVE

Kidney Health Initiative Announces Pioneer Members and Two New Projects

ASN partnered with the Food and Drug Administration in September 2012 to form the Kidney Health Initiative (KHI), which aims to work with organizations in the kidney health arena to foster innovation and ensure patient safety.

KHI is now pleased to announce the initiative's 65 Pioneer Members. This category of membership (Pioneer) was established to highlight the initial support of patient groups, professional organizations, industry partners, and research institutions based on their enrollment by December 31, 2013.

As a member-driven initiative, KHI will use its resources to develop and implement projects that are submitted by KHI members. During the first project submission cycle in

September 2013, nine project proposals were suggested by the membership. From these initial submissions, two new projects were endorsed by the KHI Board of Directors. Several other projects and ideas are at different stages of development in the pipeline and KHI expects a steady stream of projects that will have an impact on kidney disease. All KHI projects will be implemented by volunteer workgroups and a call for each workgroup is announced on the KHI website.

The KHI Board of Directors is pleased to announce the next two KHI projects:

- Workshop to Elucidate Role of Patient Preferences in Support of Center for Devices and Radiological Health (CDRH) Regulatory Actions in Kidney Disease

- Clinical Trial Endpoints in Dialysis Vascular Access

To learn more about these projects, visit KHI online at www.kidneyhealthinitiative.org.

KHI will continue to gather ideas for projects via an online web portal with two submission cycles planned for 2014 (spring and fall). The portal provides KHI members with an opportunity to submit brief project proposals and also to discuss and refine submissions through this online forum. ASN members may submit project ideas for KHI by contacting the appropriate ASN Advisory Group.

Learn more about KHI or enroll as a member by contacting KHI staff khi@asn-online.org.

Kidney Health Initiative Pioneer Members

(as of January 27, 2014)

Device Manufacturers

C.R. Bard
Medtronic
NxStage Medical Inc.
W.L. Gore & Associates

Dialysis Providers

DaVita
Dialysis Clinic, Inc. (DCI)
Fresenius Medical Care
PeaceHealth Dialysis Center (Longview, WA)

Foundations

Institute Kidney Foundation of Delhi
JDRF International
PKD Foundation
The NephCure Foundation

Health Professional Organizations

American College of Clinical Pharmacy (ACCP)
American Nephrology Nurses Association (ANNA)
American Society for Apheresis (ASFA)
American Society of Diagnostic & Interventional Nephrology (ASDIN)
American Society of Nephrology (ASN)
American Society of Pediatric Nephrology (ASPN)
American Society of Transplantation (AST)

Association for the Advancement of Medical Instrumentation (AAMI)
European Renal Association – European Dialysis and Transplant Association (ERA-EDTA)
National Renal Administrators Association (NRAA)
Nephrology Nursing Certifications Commission (NNCC)
Renal Physicians Association (RPA)
Vascular Access Society of the Americas (VASA)
Vascular Access Society

Patient Organizations

American Association of Kidney Patients (AAKP)
Dialysis Patient Citizens (DPC)
Home Dialyzers United
National Kidney Foundation (NKF)
Renal Support Network (RSN)
Vasculitis Foundation

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Detective Nephron

Detective Nephron, world-renowned for expert analytical skills, trains budding physician-detectives on the diagnosis and treatment of kidney diseases. L.O. Henle, a budding nephrologist, presents a new case to the master consultant.



Nephron What do you have for us today, my dear apprentice?

Henle A 24-year-old woman with hematuria and acute rise in creatinine level.

Nephron I see that you have taken a break from the electrolyte disorders and moved to the world of glomerular disease again. This is why nephrology is so much fun. It has so much variety to offer to us diagnosticians.

Henle Hmmm... getting back to the case, she was in her usual state of health until a few weeks ago, when she started noticing unexplained joint pains, weight loss, and a feeling of uneasiness. She also noticed subjective fevers.

Nephron What is her creatinine level now?

Henle It was 0.7 mg/dL four months ago and 1.2 mg/dL two months ago. Now it is 3.8 mg/dL.

Nephron OK; did you examine her urine?

Henle Yes, of course I did. There are a few red blood cells and many white blood cells. The red cells are dysmorphic, but no red cell casts that I could notice, and no signs of any granular casts.

Nephron Is there any proteinuria?

Henle Yes, 2 grams in a 24-hour urine collection.

Nephron I am sure they did serologies before they called you.

Henle Here are the results: antinuclear antibodies (ANA), anti-double-stranded DNA, myeloperoxidase (MPO), and proteinase 3 (PR3) all negative. Her HIV test result is positive. Hepatitis B and C results are negative.

Nephron Stop right there. So you are telling me you already have a diagnosis? Why are we presenting this case, then? Sounds like you have an HIV-related glomerular process.

Henle (*wondering to himself about quick decision by Nephron*): Hmmm! I am not too sure whether this is a glomerular process.

Nephron Why is this not a rapidly progressive GN? That has five known presentations.

Henle But in this case, anti-neutrophil cytoplasmic antibodies (ANCA) is negative and HIV is positive.

Nephron My dear apprentice, you have a lot to learn still. First and foremost, can you give me this individual's medication list? Please go get that while I drink my coffee.

Henle leaves to get the information, and Nephron gets a cup of warm coffee. Henle returns after a few hours.

Nephron Please read all her medications to me.

Henle She is taking no medications.

Nephron (*shocked*): Interesting!

Henle Can we go back to the HIV test being positive? Did I mention that her CD4 is low and her HIV viral load is high! Is there a connection to the presentation?

Nephron Of course there is. HIV can present in the kidney in many ways. The most common is HIV-associated nephropathy, usually in black individuals, as collapsing focal segmental glomerular sclerosis. Given the degree of proteinuria in this case, I doubt this is HIV-associated nephropathy, but the acute renal injury favors that diagnosis. What is her race?

Henle White.

Nephron Hmmm. If we still think this is a glomerular process, then HIV-associated immune complex disease is a possibility, given her race and the hematuria and dysmorphic red cells. On biopsy this can be IgA nephropathy, membranous GN, membranous proliferative GN, and any pathologic immune complex disease. What do you think, Henle?

Henle (*confused*): Hmmm... so is that the connection? How about we start from a more basic approach? Why are we jumping into the glomerulus without a systematic approach?

Nephron I am assuming you want to go over a systematic approach to rule in and rule out other causes of acute kidney injury (AKI)?

Henle Yes... I don't think it is a prerenal condition, because her urine Na is high and FeNa is above 1 percent. I don't think it's a postrenal condition, because I personally inserted a Foley catheter, and a bladder sonogram shows no significant residual volume. She is not oliguric. That leaves us with intrarenal causes. A tubular cause is still possible, regardless of the hematuria and proteinuria. This could be garden-variety tubular necrosis, but I can't find any source of low blood pressure or any toxic medications. An interstitial cause still bothers me. She has a lot of white blood cells in her urine, and the result of her urine culture is negative, which suggests a sterile pyuria. She might have an acute interstitial nephritis, and the proteinuria could be of tubular origin. I don't think she has a vascular disease process, although her platelets are low and she has anemia. Perhaps we should check her lactate dehydrogenase and haptoglobin levels to make sure there is no thrombotic microangiopathy from HIV? You already discussed the glomerular causes. To help distinguish from HIV-associated nephropathy and HIV-associated immune complex disease, I might get complement levels as well.

Nephron Amazing thought process, Henle. I am proud of you! Regardless, go ahead, and let's get some answers with the tests you ordered. Also, do you think a renal sonogram might help?

Henle I suppose. Why not? The size of the kidney might give us a clue regarding a differential diagnosis.

Henle exits.

Nephron (to himself): Fine work by Henle.

A day later:

Henle She is not doing well. Her renal function, anemia, and thrombocytopenia are worsening. Her complements are normal. Her renal sonogram shows massively enlarged hyperechoic kidneys: 23.5 cm bilaterally in the longitudinal axis. To me, the large size suggests HIV-associated nephropathy, amyloidosis, obstruction, or some combination—but she does not have an obstruction. Another possibility is diabetic disease, but she doesn't have long-standing diabetes. But a size over 20 cm sounds rather large to me.

Nephron Let me complete your differential. Her lactate dehydrogenase level is likely above 1000 U/L, and one more process can create this enormous kidney size. Please examine her for lymphadenopathy.

Henle, puzzled, leaves the room but returns quickly.

Nephron And?

Henle No lymph nodes anywhere, neither on examination nor on imaging. I scheduled her for a kidney biopsy.

Nephron Henle, your initial hunch was correct. You were thinking of causes of sterile pyuria and came up with interstitial nephritis? What else can cause leaking of white blood cells into the urine and interstitial nephritis and large kidneys?

Henle Infiltrative disease?

Nephron Yes, please get a kidney biopsy as soon as possible. I suspect a hematologic neoplasm.

Henle leaves the room in a rush and returns a day later.

Nephron And?

Henle Large B cell lymphoma infiltrating the kidney is the final diagnosis.

Nephron (with confidence): Infiltrating lymphoma in the kidney can lead to large kidneys, sterile pyuria, and AKI, as in this case. In addition, the proteinuria might have been tubular in origin, given that the glomeruli appear normal.

Henle is stunned.

Nephron My dear apprentice, the kidney is the most common extranodal site for lymphoma infiltration. Usually it is bilateral, and symmetric large kidneys can be seen.

Henle (puzzled): But presenting only in the kidneys and in no other place? Is that possible?

Nephron Yes, that has been reported as well: primary renal lymphoma. In addition, in autopsy studies of patients with lymphoma, renal involvement ranged from 6 percent to 60 percent of the cases. Hence, it might be clinically silent and perhaps more common than we think. Painless hematuria, nonnephrotic proteinuria, and large kidneys in a patient with lymphoma should prompt one to think about lymphoma infiltrating the kidney (LIK). Non-Hodgkin's lymphoma is the most common primary malignancy.

Henle Is AKI that common with LIK?

Nephron AKI occurs in only around 0.5 percent of all cases of LIK; hence it is not that common. And what happens? The mechanism by which lymphomatous infiltration causes renal failure is not known. It has been postulated that dense tumor infiltration of the kidney parenchyma may cause compression of the tubular lumen, producing intrarenal obstruction. In our case, it led to interstitial nephritis, but tubular necrosis can also be seen.

Henle I assume treatment with chemotherapy will reverse this quickly?

Nephron What are you waiting for?

Henle leaves to discuss the case with his hematology colleagues. A few weeks later:

Henle What a dramatic response. After chemotherapy was initiated, the patient's renal function improved, and her proteinuria and hematuria resolved. In addition, I repeated a sonogram, and the kidneys are now 16 cm bilaterally. This is amazing!

Nephron Well done, apprentice. Keep an open mind. Again, with a renal disorder you diagnosed a systemic disease that saved this patient's life. Onconeurology is an important part of nephrology that deals with cancer, chemotherapy, and the kidney. Most nephrologists should be familiar with the effects of cancer on the kidney. Cancer rates are rising, and newer chemotherapeutic agents are being used, and with this we are likely to see more renal injuries. Henle, let's get a cup of my favorite coffee. ●

Detective Nephron was developed by Kenar Jhaveri, MD, associate professor of medicine at Hofstra North Shore LIJ School of Medicine. Special thanks to Dr. Rimda Wanchoo, assistant professor of medicine at Hofstra North Shore LIJ School of Medicine, for her editorial assistance. Send correspondence regarding this section to kjhaveri@nshs.edu or kdj200@gmail.com



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