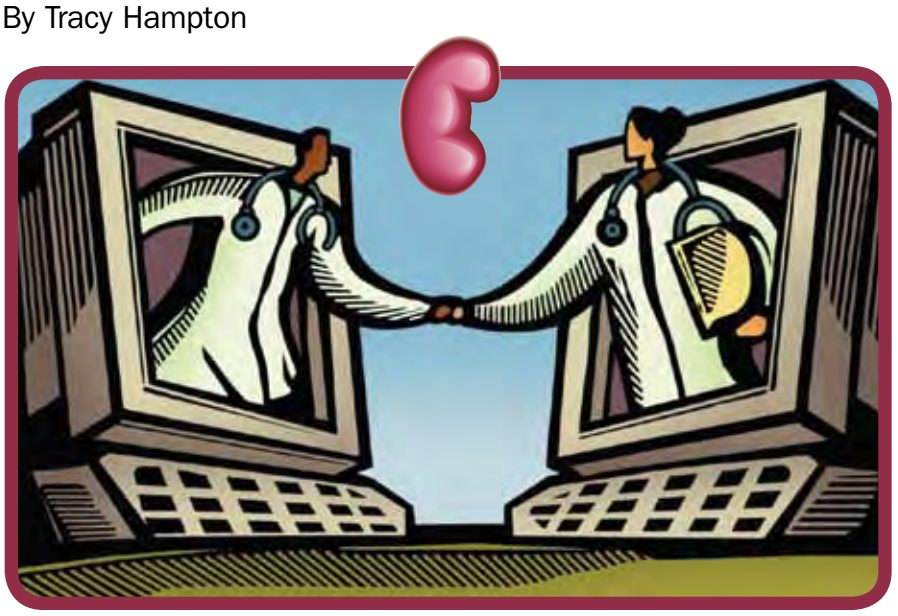
ASN LEADING THE FIGHT AGAINST KIDNEY DISEASE

# Kidney News

February 2011 | Vol. 3, Number 2

## Primary Care Physicians and Nephrologists Favor Collaboration in Kidney Disease Care

By Tracy Hampton



Collaboration between primary care physicians (PCPs) and nephrologists in the care of patients with chronic kidney disease (CKD) is widely advocated, but how do these clinicians prefer to collaborate? That was the focus of recent research on CKD care (Diamantidis CJ et al. Primary Care-Specialist Collaboration in the Care of Patients with Chronic Kidney Disease. *Clin J Am Soc Nephrol*, February 2011).

"We were able to highlight how primary care providers and nephrologists differ on certain aspects of the care of patients with chronic kidney disease," said first author Clarissa Jonas Diamantidis, MD, of the University of Maryland Medical Systems. "We were also able to identify potential barriers to collaboration among primary care providers and nephrologists."

### Nephrologists versus PCPs

Communication between PCPs and specialists in the care of patients with chronic illnesses has been linked with improved clinical outcomes, but collaborative care models for CKD across the United States have been limited.

"There are examples of successful multidisciplinary CKD teams including PCPs, nephrologists, nurses, pharmacists, social workers, and dieticians, but we have a long way to go in the U.S. to develop and test these models of care and determine if they are

*Continued on page 3*

## *Researchers, FDA, and Industry Convene with NIH to Address Acute Kidney Injury*

By Rachel Shaffer

Novel interventions and therapeutic agents being developed by academia and the pharmaceutical industry hold promise for the prevention and treatment of acute kidney injury (AKI). But questions about the design of clinical trials for these agents must be addressed before nephrologists can begin to study the therapies—and bring them to patients.

Nephrology researchers and clinicians met with National Institute of Diabetes, Digestive and Kidney Disease (NIDDK) staff, industry representatives, and Food and Drug Administration (FDA) officials in December at the "AKI Clinical Trial Design Workshop," organized and hosted by the NIDDK.

AKI is a common condition associated with high mortality, increased morbidity, and increased risk of chronic kidney disease acceleration to end stage renal disease (ESRD). A highly complex condition, AKI can be caused by one or multiple factors including trauma, compromised blood flow to the kidneys, and infections or nephrotoxins (including therapeutic agents) in the bloodstream.

Besides volume administration and renal replacement therapies, existing

*Continued on page 4*

## Inside

**KN goes mobile** Download your free app through Apple now!

# NOW AVAILABLE

## Hectorol® 2 mcg/mL vial

Announcing the availability of a second option for Hectorol® (doxercalciferol injection). In addition to the 4 mcg/2 mL vial, the Hectorol 2 mcg/mL vial is now available from Genzyme. The 2 mcg and 4 mcg vial formulations are single-use and contain no latex.

NDC # 58468-0126-1


Representative image. Not actual size.

**Indication:** Hectorol Injection (doxercalciferol injection) is indicated for the treatment of secondary hyperparathyroidism in patients with Chronic Kidney Disease on dialysis.

**Important Safety Information:** • Hectorol is contraindicated in patients with a tendency towards hypercalcemia or current evidence of vitamin D toxicity • Overdosage of any form of vitamin D is dangerous • Acute hypercalcemia may exacerbate tendencies for cardiac arrhythmias and seizures and may potentiate the action of digitalis drugs • Chronic hypercalcemia can lead to generalized vascular and soft tissue calcification • Pharmacologic doses of vitamin D and its derivatives should be withheld during Hectorol treatment to avoid possible additive effects and hypercalcemia • Magnesium-containing antacids and Hectorol should not be administered concomitantly

• Adverse effects of Hectorol treatment are: hypercalcemia, hyperphosphatemia, hypercalciuria, and oversuppression of iPTH • Adverse events reported by ≥ 5% of the Hectorol-treated dialysis patients included: headache, malaise, bradycardia, nausea/vomiting, edema, dizziness, dyspnea, and pruritus.

Please see brief summary of prescribing information on the page adjacent to this advertisement.

For more information call **1-800-847-0069** or visit **www.hectorol.com**.



HECTOROL®
doxercalciferol injection

# Collaboration

*Continued from page 1*

cost-effective," said Wendy St. Peter, PharmD, of the University of Minnesota and the U.S. Renal Data System & Chronic Disease Research Group.

To assess physicians' desires to collaborate, their preferred content of collaboration, and their perceived barriers to collaboration, Dr. Diamantidis and her colleagues had 124 PCPs and 120 nephrologists fill out a questionnaire describing the care of a hypothetical patient with progressive CKD. The investigators found that most physicians (85 percent of PCPs and 94 percent of nephrologists) desired collaboration and preferred that PCPs play a significant ongoing role in care. The most frequently desired types of input from nephrologists in collaborative care were: 1) confirmation of PCPs' appropriate clinical evaluation, 2) guidance regarding additional evaluation and testing, 3) medication regimen advice, and 4) nutritional advice.

Nephrologists were more likely than PCPs to report they had sufficient ancillary support for the care of their patients with CKD and that they felt the medical care they provide was helpful in slowing CKD disease progression. They also were less likely to perceive insurance as a barrier to nephrology referral. More than half of nephrologists felt that patients were referred too late, and nearly one-third felt patients seen in consultation were taking inappropriate medications.

Nephrologists were more likely than PCPs to prefer collaboration focusing on predialysis/renal replacement therapy preparation (73 percent versus 52 percent) and electrolyte management (81 percent versus 46 percent). PCPs were more likely to desire collaboration if the hypothetical patient had both diabetes and hypertension, rather than hypertension alone; if they believed the care they provide helps slow CKD disease progression; and if they did not perceive health insurance as a barrier to referral to a nephrologists.

## Future directions

The study's findings could have important clinical applications, as PCPs often misjudge the severity of CKD or refer patients to nephrologists so late that interventions to slow CKD progression or prepare patients for renal replacement cannot be implemented in a timely manner.

"As medical conditions become more complex and health care reform takes effect, primary care providers and specialists must work together more and more to provide optimal care to patients. Identifying physicians' perspectives on how that care should be provided is the first step in a process that will ultimately lead to improved quality of care and patient outcomes," said Diamantidis.

Others in the field say the research offers important information and should stimulate additional investigations.

"This study suggests that it would be worthwhile to develop and evaluate new multidisciplinary collaborative care models to optimize care in CKD patients," said St. Peter. She added that addressing barriers to collaboration will also be important.

"The study provides some insights into the different perceptions between PCPs and nephrologists as to what the patient needs truly are, and how best to meet them. There is a need for us as health care providers not only to understand the information requirements of each other, but also to engage patients in what their expectations are," said Adeera Levin, MD, FRCPC, a professor in the division of nephrology at the University of British Columbia, in Vancouver, Canada.



## Letters

***ASN Kidney News* accepts letters to the editor in response to published articles. Please submit all correspondence to kidneynews@asn-online.org**

ASN LEADING THE FIGHT AGAINST KIDNEY DISEASE

# Kidney News

**Editorial Staff**
**Editor-in-Chief:** Pascale H. Lane, MD, FASN
**Managing Editor:** Dawn McCoy
**Design:** Lisa Cain



*ASN Kidney News* is published by the American Society of Nephrology
1725 I Street NW, Suite 510, Washington, DC 20006. Phone: 202-659-0599

www.asn-online.org



Postmaster: Please send address changes to *ASN Kidney News*, c/o Customer Service, American Society of Nephrology 1725 I Street NW, Suite 510, Washington DC 20006.

Publications mail agreement No. 40624074. Return undeliverable Canadian addresses to PO Box 503, RPO West Beaver Creek, Richmond Hill ON L4B 4R6

*ASN Kidney News* (ISSN print 1943-8044 and online 1943-8052) is an official publication of the American Society of Nephrology, 1725 I Street NW, Suite 510, Washington DC 20006, and is published monthly. Application to mail as Periodicals Postage Pending at Washington, DC, and at additional mailing offices. Subscription rates: $12 per year. To order, please email bhenkel@asn-online.org. Subscription prices subject to change. Annual ASN membership dues include $12 for *ASN Kidney News* subscription.



## Acute Kidney Injury

*Continued from page 1*

strategies to reduce the morbidity and mortality of patients with AKI are inconclusive or generally not effective. The workshop provided a unique forum for stakeholders across the AKI treatment spectrum—from basic researchers to industry and regulators—to brainstorm potential new therapeutic compounds, drug targets, and optimal clinical trial designs for AKI.

"Not only did this workshop help us in the nephrology research community better understand what the FDA and industry need and want from us, it sets the stage for more communication in the future—which will hopefully translate to more treatments reaching AKI patients faster," said Paul Palevsky, MD, who assisted in organizing the workshop.

A well-designed clinical trial with appropriate endpoints is necessary for successful translation of a therapy from the bench to the bedside. Trials must meet not only researchers' scientific and methodological standards, but also those of industry (which would make the product available to patients) and the FDA (which must approve the drug). Workshop participants debated where to set clinical endpoints—or a composite endpoint—that could be shared and recognized as acceptable by researchers, the FDA, and industry, in a manner widely agreed as open and transparent. Industry representatives also discussed the limitations, needs, and barriers they face.

"Everyone understood that we cannot continue to work in silos but rather progress depends upon cooperation among the stakeholders," said Mark Okusa, MD, chief of the division of nephrology and director, Center for Immunity, Inflammation and Regenerative Medicine at the University of Virginia in Charlottesville. "This highlighted the necessity of collaboration—and an important role for the NIH Public Private Partnership Program in facilitating these interactions."

National Institutes of Health (NIH) Public Private Partnership Program (PPP) staff also participated in the workshop. The PPP facilitates collaborations between the NIH and other organizations including professional societies, industry members, and academic institutions to improve public health though research. The PPP also provides mechanisms by which AKI researchers and industry members at the workshop could identify shared areas of interest and conduct studies that NIH might not otherwise be able to support (see sidebar).

Among the most important issues facing clinical trial design is identifying approaches to mitigate the financial challenges NIH and industry face in conducting the trials. One potential solution workshop participants identified is to pool similar placebo-treated patients from different Phase II studies into a large protected database available for determination of event rates and other parameters. Such information is essential to the design and implementation of appropriately powered Phase III studies.

The workshop was in part the result of conversations between the NIDDK and the ASN AKI Advisory Group.

"ASN was an important force in convincing NIH that we have important tools and therapies to examine," said NIDDK Acute Kidney Injury Program Director Paul Kimmel, MD, FASN, in his opening remarks. "This [workshop] was a direct result of ASN dialogue with NIDDK."

"The AKI Advisory Group was challenged by NIH staff to delineate up-and-coming therapies for AKI that would provide the stimulus for—and benefit from—a workshop to facilitate interactions between an array of AKI stakeholders," said Bruce Molitoris, MD, FASN, chair of the nephrology division at Indiana University School of Medicine and ASN's AKI Advisory Group Council Liaison. "The NIH then worked diligently to deliver an outstanding meeting based on an environment of understanding, cooperation and respect. Participants left exhausted and exhilarated."

## Public-Private Partnerships

In an effort to foster better working relationships between government and industry, the National Institutes of Health (NIH) initiated a program on public-private partnerships (PPP) in 2005. Housed under the Office of Science Policy, the PPP works to "facilitate collaborations that improve the public health through biomedical research."

Although the research benefits of the collaboration of NIH with private industry are well established, at times structuring these partnerships has proven cumbersome. The PPP acts as a central coordinator helping to aid communication, establishing a set objective for the partnership, and organizing the parameters of the collaboration.

An example of a recent collaboration facilitated by the PPP is the Biomarkers Consortium, consisting of the NIH, the Food and Drug Administration, the Centers for Medicare & Medicaid Services, as well as private industry and nonprofit advocacy groups. The project works to speed the identification, testing, and regulatory acceptance of biomarkers. The existence of the PPP allowed the diverse stakeholders involved in the biomarkers consortium to work collectively toward a shared goal of advancing patient health through new diagnostic tools, technologies, and treatments.

# 2010 Corporate Supporters

ASN LEADING THE FIGHT AGAINST KIDNEY DISEASE

ASN gratefully acknowledges the Society's Diamond and Platinum Level Corporate Supporters for their contributions to 2010.

## Diamond Level

Abbott
A Promise for Life

AMGEN

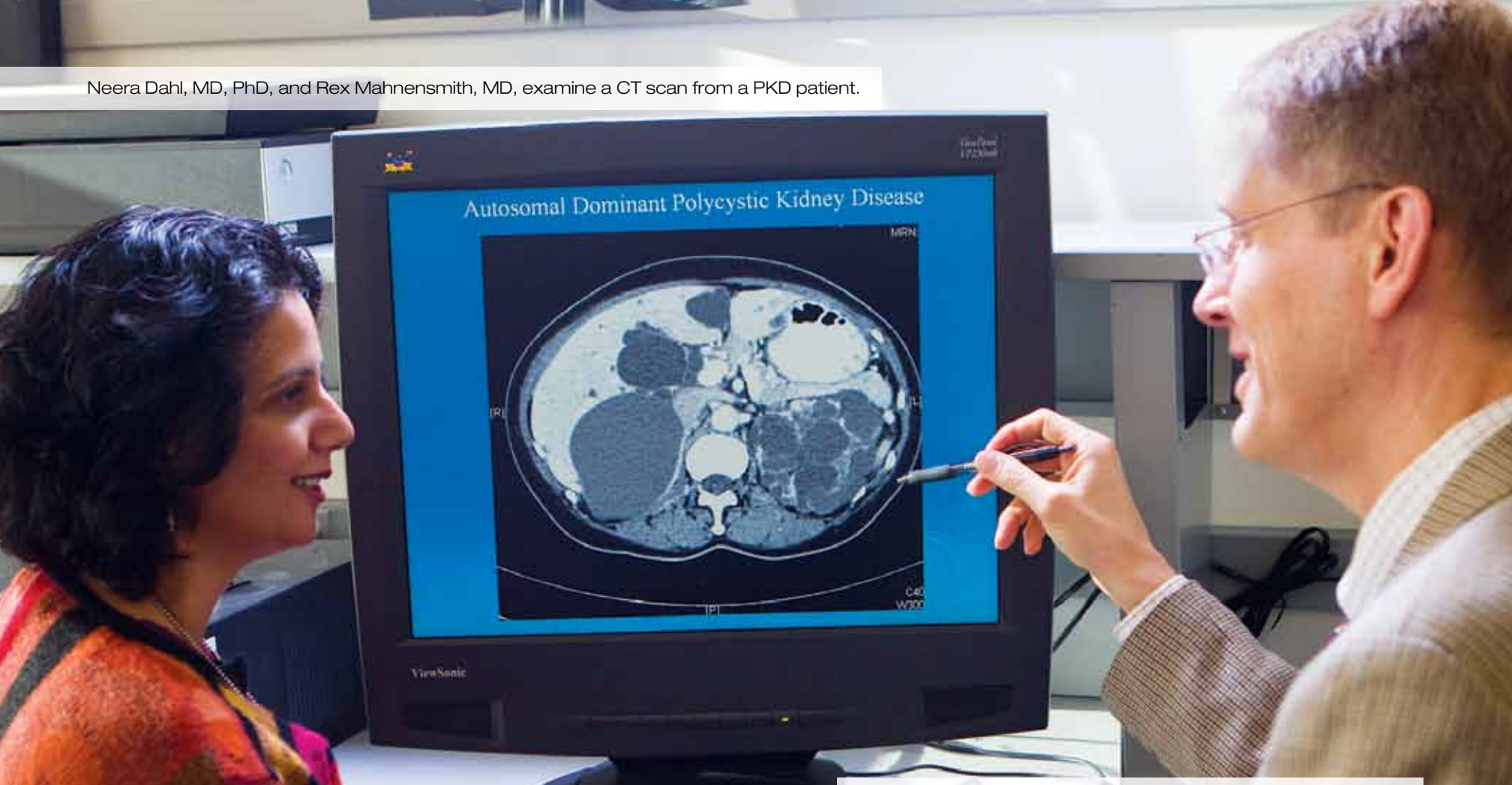
genzyme

Otsuka
Otsuka America Pharmaceutical, Inc.

REATA
PHARMACEUTICALS

## Platinum Level

Fresenius Medical Care




Neera Dahl, MD, PhD, and Rex Mahnensmith, MD, examine a CT scan from a PKD patient.

# Research Excellence, Clinical Leadership and a Commitment to Our Patients

Yale-New Haven Hospital is the primary teaching hospital of Yale School of Medicine. Kidney disorders services at Yale-New Haven were ranked 33rd by *U.S.News & World Report* in 2010.

The genetics behind kidney disease are intricate and multi-faceted. Only a few medical institutions in the country have the commitment to understanding and treating inherited kidney diseases and the resources to house the prestigious George M. O'Brien Kidney Research Center and a Polycystic Kidney Disease (PKD) Research Center, all supported by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). We are one of those centers.

Our researchers have discovered over fifteen genes for human diseases affecting the kidney and blood pressure. These discoveries cover the gamut from rare disorders of blood pressure regulation through sodium and potassium handling such as Liddle's syndrome, pseudohypoaldosteronism type II and Bartter's and Gittelman's syndromes to such common inherited kidney diseases as polycystic kidney disease (PKD). While our researchers are now seeking to translate these findings to treatments for PKD and other disorders, our nephrologists are using these discoveries to help our patients lead healthy and fulfilling lives.

Being at the forefront of clinical research and treatments means that our physicians and surgeons are furthering the current understanding of kidney disease. Most importantly, it means they are positioned to provide the best care possible to our patients.

Yale-New Haven Hospital

www.ynhh.org

## Geriatric Kidney Care

ASN Kidney News *thanks editorial board member Edgar Lerma, MD, of the University of Illinois at Chicago College of Medicine for editing this special issue.*

# Kidney Care in the Elderly:

## ASN's Geriatric Nephrology Educational Initiatives and Advisory Group on Geriatric Nephrology Speak Out

By Dimitrios G. Oreopoulos and Jocelyn Wiggins

U.S. census data show that the population of individuals over 65 in the United States is growing rapidly and is expected to double over the next 20 years. This means that current fellows can expect to see an increasing number of older patients in professional practice. Average life expectancy is currently around 75.2 years for men and 80.4 years for women, and continues to rise. During the 1990s, the fastest growing population was that of individuals over 85, with 38 percent annual growth, and this group is the largest consumer of health care services.

Of the 35 million people over 65 in the United States, 40 percent have some level of disability relating to sensory, physical, mental, or self-care capacity. Disability greatly impacts the ability of these patients to follow a complex medical regimen, such as that recommended for patients with chronic kidney disease (CKD). Many patients in this age group have lost the ability to administer their own pills, to buy and cook their own groceries, or to drive themselves to office visits or dialysis units. Many other patients, particularly those with diabetes, have difficulties with basic mobility. Coresh et al. have estimated that the overall prevalence of CKD has increased from 10 to 13 percent in the U.S. adult population since 1988, and that most of that growth has occurred in the older population.

The management of elderly patients who require chronic dialysis is even more complex. These individuals frequently have more difficulty with vascular access and more cardiovascular disease that leads to arrhythmias and hypotension while on dialysis. Furthermore, traveling to and from the unit is a greater burden to them. The U.S. Renal Data System has reported that the peak incidence of treated end stage kidney disease (ESKD) has shifted from the 70- to 79-year-old age group, where it has been for the last 15 years, to the 80- to 85-year-old age group (Figure 1). This brings geriatric patients squarely into the domain of the nephrologist.

This demographic imperative prompted the Accreditation Council for Graduate Medical Education (ACGME) to issue a directive on geriatric education for nephrology trainees. This mandate, published in 2008, states that "fellows must have formal instruction, clinical experience and demonstrate competence in the prevention, evaluation, and management of geriatric aspects of nephrology." Prior to this there had been a number of efforts to promote geriatric nephrology that unfortunately were not very successful. We will describe these efforts to provide a backdrop for the subsequent increase in interest in geriatric nephrology through the American Society of Nephrology (ASN).

In May 1985, the first International Conference of Geriatric Nephrology was held in Toronto. The event drew over 500 attendees who brought with them a tremendous enthusiasm about geriatric nephrology. As a result of this successful meeting, a number of individuals created the International Society for Geriatric Nephrology and Urology with its own *Journal for Geriatric Nephrology and Urology*, a forum to exchange ideas, experiences, and resulting research on geriatric nephrology.

Five additional international meetings of this society took place in cities around the world: Salamanca, Spain, organized by Juan Macias-Nunez; Lisbon, Portugal, organized by Fernando Carrera; Atlanta, organized by Nancy Kutner; Thessaloniki, Greece, organized by Nicholas Dombros; and Antalya, Turkey, organized by Fevzi Ersoy. The past presidents of the International Society for Geriatric Nephrology are Dimitrios Oreopoulos of Toronto, Michael Michelis of New York, and Eli Friedman of New York. Francesco Locatelli of Italy is the current president of this society.

In spite of these efforts, interest among nephrologists concerning geriatric nephrology did not increase and, if anything, decreased. Membership to the society and participation at meetings declined and subscriptions and submissions to the journal were not sufficient to sustain it. As a result, the publisher decided to incorporate the journal into a new journal (International Urology and Nephrology), which is now the official *Journal of the International Society for Geriatric Nephrology* and features a section on geriatric nephrology. The editor-in-chief of *International Urology and Nephrology* is Dimitrios Oreopoulos.

While these movements and changes were occurring internationally, the Franklin William Scholarship Program, sponsored by the Association of Specialty Professors and funded by the J.A. Howard Foundation and Atlantic Philanthropies, was launched in the United States in 2002 to encourage a new generation of nephrologists with an expertise in geriatric nephrology. Today they have partnered with 11 professional societies, including the ASN, and fund two Two-Year Career Development Awards for junior faculty who are willing to be mentored in geriatrics and devote some of their research efforts to aging-related problems. A total of 10 nephrologists have taken advantage of this program and completed it. We hope that these young nephrologists will be the leaders in geriatric nephrology in the future.

The National Institutes of Health (NIH) has also recognized the growing importance of kidney disease in the aging population and sponsored two workshops to address what is known about kidney disease in the elderly and to identify research gaps and make priorities for resources to address them. The first workshop, held in May 2008, focused on chronic kidney disease in the older adult. Recommendations from this workshop appear in an article in the *Journal of the American Society of Nephrology* with Sharon Anderson as lead author (1). As a result of this workshop, the NIH will provide grants for research on renal function and chronic kidney disease in aging that will be open until 2012. The second workshop, held in May 2010, focused on acute kidney disease in older adults. A follow-up summary of the group's recommendations has been accepted for publication and will appear shortly in the *Journal of the American Society of Nephrology*. It is anticipated that there will be further program announcements linked to this topic.

*Continued on page 8*

# Kidney Care in the Elderly

*Continued from page 7*

## Mandated training in geriatric nephrology and the role of the ASN

The ACGME's mandate that there should be formal instruction in geriatric nephrology for nephrology trainees spurred an interest in geriatric nephrology that has been enhanced not only by the increasing number of dialysis patients but also the increasing number of elderly patients referred to nephrologists because of impaired estimated glomerular filtration rate (eGFR). Nephrologists are now inundated by referrals for elderly patients to their clinics, and the number of elderly patients over 75 in dialysis units is increasing exponentially, forcing nephrologists who have no formal training in geriatrics to practice as amateur geriatricians.

In response to these increases, the ASN invited a group of individuals to form a committee to design a curriculum for teaching geriatric nephrology by identifying topics and authors to write chapters on these topics. The 38 chapters are available free of charge on the ASN website (http://www.asn-online.org/education_and_meetings/geriatrics/).

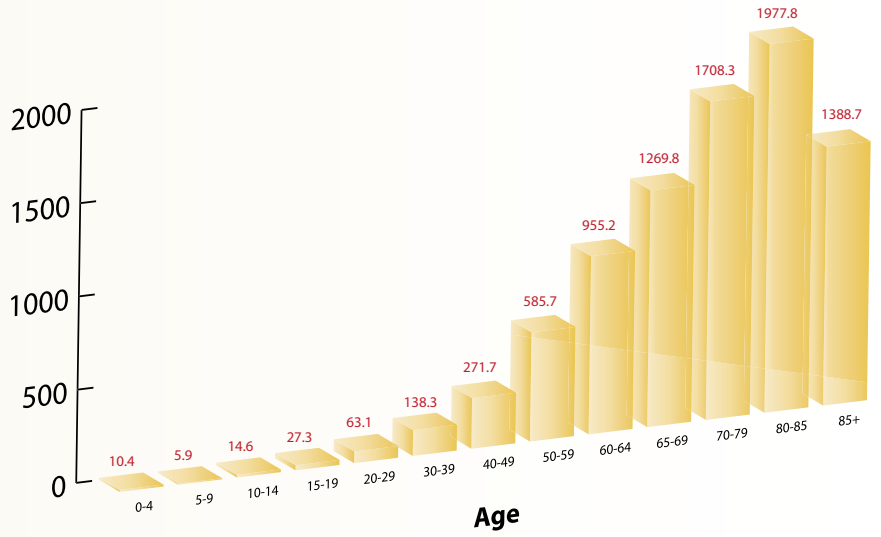
To promote this educational material, the ASN invited the group to organize a two-day course on geriatric nephrology for Renal Week that has been presented successfully for the years 2008, 2009, and 2010. In the first two years, the authors of the curriculum presented their chapters. Their presentations were audiotaped and are now available at the website mentioned previously.

The ASN Council also invited the creation of the Advisory Group on Geriatric Nephrology (AGGN) to advise the council on issues related to geriatric nephrology. The members of this group are Dimitrios Oreopoulos (co-chair), Richard Glassock, Jocelyn Wiggins (co-chair), Gary Striker, Ann O'Hare, Mitchell Rosner, Vanita Jassal, Mark Williams, Nicole Stankus, Nobuyuki Miyawaki, Mark Swidler, Manjula Tamura, and Mark Unruh.

The AGGN has already made recommendations to the ASN Council for the addition of key words related to aging, biology, and older adults when authors submit abstracts to the ASN program. They have also recommended the institution of an aging section for presentations and posters and an aging track on program participants who wish to seek out related presentations.

Additionally, the AGGN applied for a grant from the National Institute on Aging that has been approved to fund travel for 25 fellows to attend the course in geriatric nephrology during Renal Week 2010. The AGGN also plans to reach out to other societies. An application to the Association of Specialty Professors for a grant toward organizing events in these societies with emphasis on geriatric nephrology is under consideration. The aim is to partner with other societies at annual professional meetings and raise awareness about the special challenges of older people with kidney disease. Such societies include the American Geriatric Society and the Society of General Internal Medicine and Family Medicine.

**Figure 1. Incident rates of treated end stage kidney disease**




## Special issue of the Nephrology Self-Assessment Program on geriatric nephrology

The highlight of the AGGN's activity to date has been the preparation of a special issue of the *Nephrology Self-Assessment Program* (NephSAP) on geriatric nephrology in January/February 2011.

Topics of this issue include:

- Introduction to the biology of aging and the kidney
- Age, eGFR formulas, and assessment of risk for adverse cardiovascular and renal outcomes in CKD
- Geriatric hypertension
- Diabetic kidney disease in the elderly
- Glomerular diseases
- Acute kidney injury (Rosner)
- Therapeutic options for older individuals with CKD
- Palliative care and geriatric management of patients with advanced CKD

We expect that this issue will be an important milestone in promoting geriatric nephrology and will contribute to the appropriate care of many elderly patients with chronic renal disease. We are grateful to the editors of NephSAP for agreeing to publish such an issue.

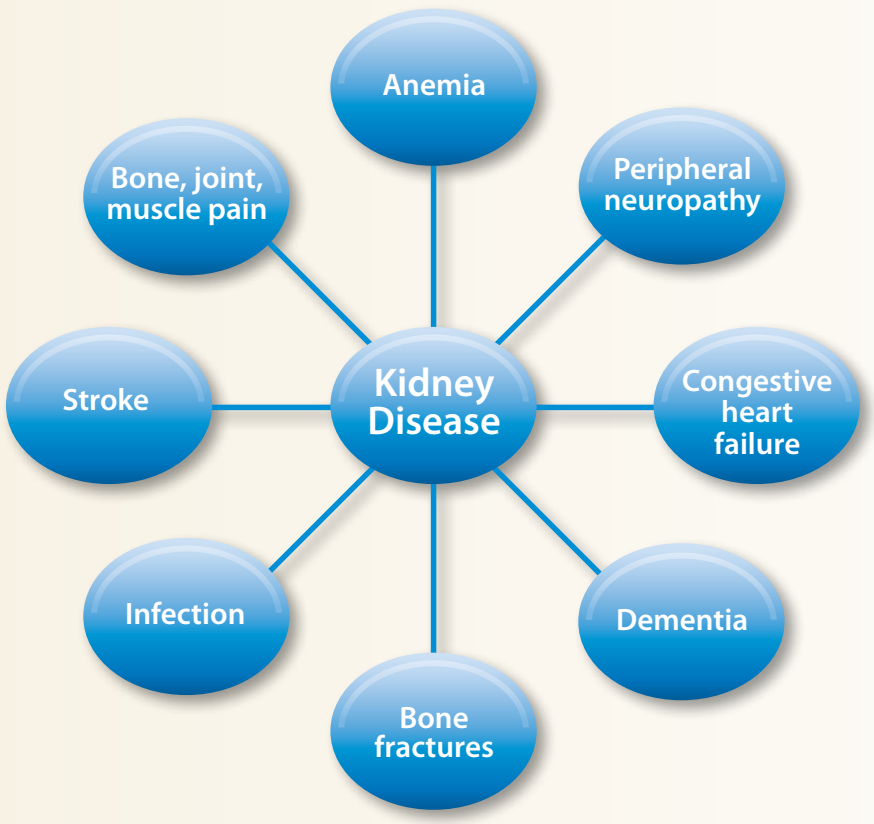
The activities of the AGGN will continue in the future with the overarching goal of promoting education on all issues related to geriatric nephrology, and thus improving the care of elderly patients with kidney disease.

**References**

1. Anderson S, et al. Prediction, progression, and outcomes of chronic kidney disease in older adults. *J Am Soc Nephrol* 2009; 20:1199–1290.

*Dimitrios G. Oreopoulos is affiliated with the University of Toronto and Toronto Western Hospital in Toronto, ON. Jocelyn Wiggins is affiliated with the University of Michigan in Ann Arbor, MI.*

**Kidney Disease Increases Risk of the Following Conditions:**




## ASN Member Joins Standards for End Stage Renal Disease Steering Committee at National Quality Forum

ASN member Jeffrey Berns, MD, FASN, has been selected to serve on the Steering Committee for Standards for End Stage Renal Disease (ESRD) at the National Quality Forum (NQF).

In September 2010, the NQF released a call for nominees to serve on the Steering Committee. ASN submitted the name of Dr. Berns, who, along with 16 other members, will oversee the creation of a draft consensus report on additional ESRD performance measures. The process will culminate in the steering committee's recommending which measures should be adopted as the consensus measures for ESRD. These recommendations will be monitored closely by the Centers for Medicare & Medicaid Services (CMS).

NQF sought nominees who represent various viewpoints and perspectives to help craft the potential consensus measures. ASN congratulates Dr. Berns on his selection and looks forward to working with NQF to identify performance measures that will ensure the highest quality of care for patients with ESRD. To read an overview and full roster for the committee, please see http://www.qualityforum.org/Projects/e-g/End_Stage_Renal_Disease_2010/End_Stage_Renal_Disease_2010.aspx?section=callfornominations2010-09-012010-09-30#t=1&s=&p)

# Acute Kidney Injury in the Elderly: A Growing Problem with Important Implications

By Steven Coca and Mitchell Rosner

Elderly persons frequently experience acute kidney injury (AKI). Although studies describing its incidence in this population are difficult to compare because definitions of AKI vary dramatically from study to study, it is clear that the elderly are at the very highest risk for developing the condition. Indeed, Feest and coworkers (1) demonstrated that there is a three- to eightfold progressive, age-dependent increase in the frequency of development of community-acquired AKI in patients over 60.

Over the past 25 years, the mean age of patients with AKI has increased by at least five years and perhaps as much as 15 years (2). Groeneveld et al. (3) demonstrated that the age-related yearly incidence of AKI rose from 17 per million in adults under age 50 to 949 per million in those ages 80–89. A nine-year, prospective study in Madrid demonstrated a 3.5-fold greater incidence of AKI in patients older than 70 (4). Most recently, Ali et al. (5) demonstrated that the average age of patients with AKI in a large European cohort was 76. The average age of patients with acute-on-chronic renal failure was 80.5 years, however, and this group had a much higher risk for adverse outcomes.

The number of patients over 80 entering the intensive care unit (ICU) has increased over time. In a multicenter study of 120,123 adult ICU admissions of more than 24 hours' duration, the Australian New Zealand Intensive Care Society Adult Patient (ANCIZS) database researchers determined that 13 percent of these patients were 80 or older, and that the admission rate for this age group increased by 5.6 percent per year over the 2000–2005 study period (6). This critically ill population is especially vulnerable to the development of AKI; for example, in the previously mentioned ANZICS database, Bagshaw and colleagues (6) found that 36.1 percent of septic ICU patients developed AKI within 24 hours of admission, and half of these patients were also elderly. A historical cohort analysis focusing on epidemiologic trends for AKI in the ICU determined that 40 percent of 381 critically ill octogenarians had a creatinine level above 1.36 mg/dL, compared with 4 percent in the period before 1978 (7).

Although all causes of AKI are encountered in this age group, prerenal and postrenal etiologies are especially prevalent in elderly patients (8). Furthermore, elderly patients are more frequently subjected to invasive procedures, exposure to multiple (and possibly nephrotoxic) medications, and to radiocontrast agents. The changes in drug metabolism and disposition that occur with aging also contribute to higher risk for drug-induced AKI (9). Although some of the increased susceptibility to the development of AKI in elderly patients can be attributed to clinical variables, specific structural, functional, hemodynamic, and cellular changes that occur with aging predispose the kidney to injury in stressful states.

## Predisposing factors to AKI in the elderly

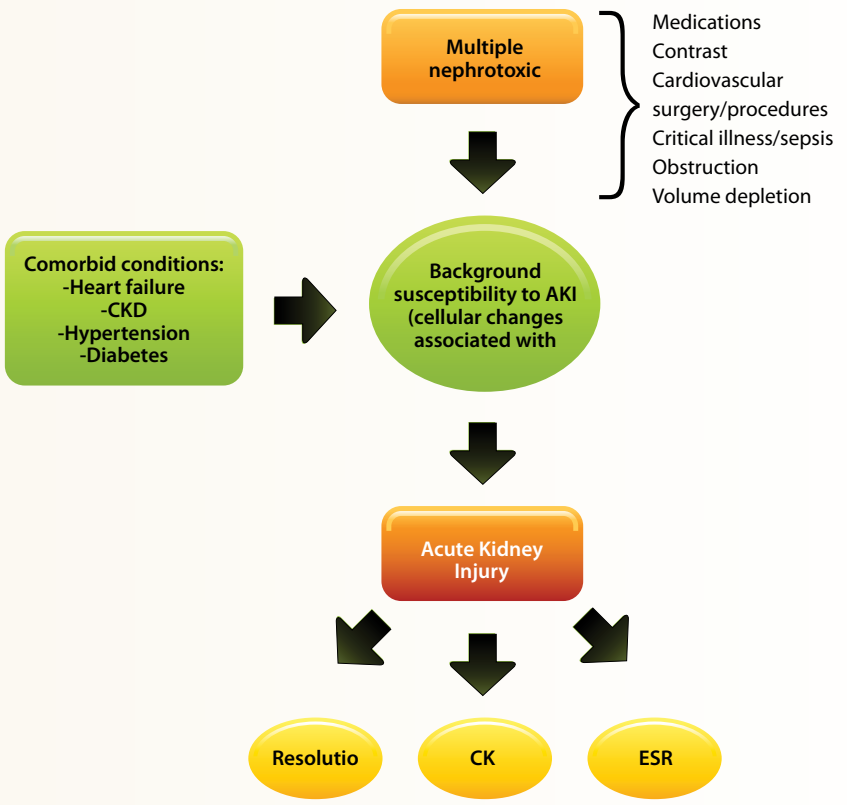
In the absence of a specific disease, the kidney undergoes age-dependent structural and functional alterations leading to a significant decrease in renal mass, functioning nephron numbers, and baseline kidney function.

Although it has been proposed that parenchymal loss in the aging kidney directly confers a higher susceptibility to acute damage, this is not universally supported by experimental data, and the picture is likely more complex. Changes in renal hemodynamics and functional reserve, specific cellular changes such as shortening of telomere length, increased expression of messenger RNA and proteins of candidate genes associated with senescence, declines in cellular antioxidant defenses with aging, and impairment of renal repair processes after injury all contribute to the increased susceptibility of the aging kidney to acute insults (10).

This background susceptibility to AKI is compounded by the numerous nephrotoxic insults to which elderly patients may be exposed (Figure 1). For instance, most elderly patients are taking multiple medications, including drugs that affect renal hemodynamics (such as angiotensin-converting enzyme inhibitors), are directly nephrotoxic (such as antibiotics or chemotherapeutic agents), or can potentiate nephrotoxicity (such as diuretics that may induce volume depletion).

Furthermore, elderly patients are more commonly exposed to potential nephrotoxic procedures such as cardiac catheterization or cardiovascular surgery, which can lead to either nephrotoxic or ischemic acute tubular necrosis. In addition, comorbid conditions such as heart failure, chronic kidney disease, diabetes, and hypertension all serve as independent risk factors for the development of AKI in the elderly. Finally, elderly patients are more susceptible to prerenal (either true volume depletion or decreased effective circulating volume) and obstructive etiologies (such as prostatic disease). Given the multitude of factors, it is not surprising that elderly patients are at the very highest risk for the development of AKI.

**Figure 1. Development and outcome of acute kidney injury in the elderly patient**




**Abbreviations: AKI = acute kidney injury; CKD = chronic kidney disease; ESRD = end stage renal disease.**

## Prevention of AKI in the elderly

Prevention of AKI in elderly patients first involves recognizing their increased vulnerability due to normal age-related decline in glomerular filtration rate (GFR) or pathologic chronic kidney disease (CKD) from multiple comorbidities that have accumulated over the lifespan. Because muscle mass decreases with age (11), it is important to calculate GFR using estimating equations (Modification of Diet in Renal Disease or CKD Epidemiology Collaboration) rather than solely evaluating the serum creatinine concentration.

Nearly 50 percent of patients 70 or older have CKD (12), which is the strongest risk factor for AKI (13). Thus, the majority of elderly patients in the ICU will need to have doses of potentially nephrotoxic drugs reduced and have prehydration strategies implemented prior to or concurrent with some agents (radiocontrast, IV acyclovir, amphotericin B, methotrexate). For patients with moderate to severe CKD that need revascularization, off-pump coronary artery bypass grafting has been demonstrated to be effective at reducing the risk for AKI (14).

With specific regard to the prevention of contrast-induced nephropathy, for high-risk patients, volumes of intra-arterial or intravenous radiocontrast should also be limited, and angiotensin-converting enzyme inhibitors and nonsteroidal anti-inflammatory drugs should be withheld, when possible. However, many of the etiologies of AKI are not easily preventable.

## Treatment of AKI

No specific therapies for the amelioration of AKI, once it is has occurred, exist for humans. Thus, the management of AKI is largely supportive, through maintenance of adequate renal blood flow, avoidance of further injury, and renal replacement support (if necessary).

The decision to initiate renal replacement therapy (RRT) in elderly persons is potentially controversial, given the possibility that older persons may not fare as well on this aggressive, life-sustaining type of therapy because of patient-based factors such as decreased cardiovascular reserve, autonomic dysfunction, and an increased

*Continued on page 10*

# AKI in the Elderly

*Continued from page 9*

tendency toward bleeding complications. Recent large randomized controlled trials comparing the intensity or modality of RRT did not perform subgroup analyses on older versus younger patients (15–17).

Studies that have directly examined a possible differential in survival by age in patients with severe AKI receiving RRT have not found any effect modification by older age on hospital survival (7, 18, 19). In fact, several studies demonstrate that mortality from AKI in elderly persons (including AKI requiring RRT) has decreased over the past several years (20–22). This phenomenon does not imply more liberal application of RRT to individuals with AKI who are less ill than past AKI sufferers; rather, the data demonstrate that the reductions in mortality over time were witnessed despite increasing comorbidity and severity of illness. Thus, there is absolutely no evidence to suggest that age alone should be a criterion for withholding acute RRT. The decision must be individualized depending on all of the factors, including the severity of illness, likelihood of meaningful physical and cognitive recovery, and family and patient wishes.

## Recovery of renal function and prognosis

The incidence of in-hospital mortality from AKI has been repeatedly shown to increase in association with the severity of AKI (23). Furthermore, several studies have demonstrated that older age itself is an independent risk factor for mortality in patients with AKI in the ICU (24–27). However, the focus in the AKI literature over the past few years has been to examine outcomes in those who survive hospital and ICU admission with AKI. Evidence suggests that more elderly individuals with severe AKI are surviving in the ICU, so the prevalence of long-term adverse consequences related to AKI may represent a substantial burden in the modern era. As with mortality risk, older age itself is associated with a greater chance of nonrecovery of renal function back to baseline after AKI by the time of hospital discharge (28).

Several recent studies have demonstrated that the long-term risk for CKD and death in survivors of AKI is much higher than those without AKI. The adjusted hazard ratio for death after AKI ranges from 1.25 to 3.2, and the adjusted hazard ratio for the development of advanced CKD or end stage renal disease (ESRD) associated with AKI is 3.2 to 41.2 (29–31).

Although animal data would suggest an increased fibrotic response in the kidney post-AKI in older versus younger individuals (32), the data from human studies is controversial with regard to whether those with AKI who are older are at higher relative risk for ESRD than younger people. Whereas one study (33) demonstrated a higher relative risk for ESRD in individuals over 65 compared with those under 65, another study (29) showed that the adjusted relative risk for ESRD declined with increasing strata of age. Because older age is clearly a risk factor for death, the relationship witnessed in the latter study may be due to the competing endpoint of death.

Few studies have actually quantified the loss of GFR over time after AKI; however, James and colleagues (34) recently demonstrated that the rate of decline in GFR after mild AKI was 1.0 mL/min/1.73 $m^2$, and 2.8 mL/min/1.73 $m^2$ after moderate or severe AKI (compared with 0.1 mL/min/1.73 $m^2$ in those without AKI). Although this cohort primarily included elderly individuals (mean age 67 years in those with AKI), the patients were not necessarily ICU patients, and thus the ability to generalize these data to the elderly ICU patient is not 100 percent certain.

With regard to absolute numbers, approximately 1.4 million patients aged 65 or older are discharged alive after an ICU admission in the United States annually (35). Because the incidence of AKI in this critically ill population is approximately 30 percent, and the incidence of ESRD after AKI is approximately 26 per 1000 person-years (29, 31), then approximately 11,000 elderly persons per year are developing new ESRD as a result of AKI in the ICU, representing nearly 11 percent of total new cases of ESRD annually in the United States (36). Thus, the focus of upcoming research endeavors should focus on identifying agents or strategies to prevent AKI, ameliorate AKI once it has occurred, and reduce the transition from AKI to CKD/ESRD. In the meantime, clinicians should be highly vigilant regarding postdischarge kidney function in the elderly patient after ICU admission.

**References**


1. Feest TG, Round A, Hamad S. Incidence of severe acute renal failure in adults: results of a community based study. *BMJ* 1993; 306:481–483.
2. Turney JH, et al. The evolution of acute renal failure, 1956-1988. *Q J Med* 1990; 74:83–104.
3. Groeneveld AB, et al. Acute renal failure in the medical intensive care unit: predisposing, complicating factors and outcome. *Nephron* 1991; 59:602–10.
4. Pascual J, et al. Incidence and prognosis of acute renal failure in older patients. *J Am Geriatr Soc* 1990; 38:25–30.
5. Ali T, et al. Incidence and outcomes in acute kidney injury: a comprehensive population-based study. *J Am Soc Nephrol* 2007; 18:1292–1298.
6. Bagshaw SM, et al. Very old patients admitted to intensive care in Australia and New Zealand: a multi-centre cohort analysis. *Crit Care* 2009; 13:R45.
7. Akposso K, et al. Acute renal failure in patients over 80 years old: 25-years' experience. *Intensive Care Med* 2000; 26:400–406.
8. Macias-Nunez JF, Lopez-Novoa JM, Martinez-Maldonado M. Acute renal failure in the aged. *Semin Nephrol* 1996; 16:330–338.
9. Jerkic M, Vojvodic S, Lopez-Novoa JM. The mechanism of increased renal susceptibility to toxic substances in the elderly. Part I. The role of increased vasoconstriction. *Int Urol Nephrol* 2001; 32:539–547.
10. Rosner MH. Acute kidney injury in the elderly. *Aging Health* 2009; 5:635–647.
11. Ohkawa S, et al. Association of age with muscle mass, fat mass and fat distribution in non-diabetic haemodialysis patients. *Nephrol Dial Transplant* 2005; 20:945–951.
12. Coresh J, et al. Prevalence of chronic kidney disease in the United States. *JAMA* 2007; 298:2038–2047.
13. Hsu CY, et al. The risk of acute renal failure in patients with chronic kidney disease. *Kidney Int* 2008; 74:101–107.
14. Nigwekar SU, et al. Off-pump coronary artery bypass surgery and acute kidney injury: a meta-analysis of randomized and observational studies. *Am J Kidney Dis* 2009; 54:413–423.
15. Palevsky PM, et al. Intensity of renal support in critically ill patients with acute kidney injury. *N Engl J Med* 2008; 359:7–20.
16. Bellomo R, et al. Intensity of continuous renal-replacement therapy in critically ill patients. *N Engl J Med* 2009; 361:1627–1638.
17. Vinsonneau C, et al. Continuous venovenous haemodiafiltration versus intermittent haemodialysis for acute renal failure in patients with multiple-organ dysfunction syndrome: a multicentre randomised trial. *Lancet* 2006; 368:379–385.
18. Pascual J, Liano F. Causes and prognosis of acute renal failure in the very old. Madrid Acute Renal Failure Study Group. *J Am Geriatr Soc* 1998; 46:721–725 .
19. Van Den Noortgate N, et al. Outcome in a post-cardiac surgery population with acute renal failure requiring dialysis: does age make a difference? *Nephrol Dial Transplant* 2003; 18:732–736.
20. Waikar S, et al. Declining mortality in patients with acute renal failure, 1988 to 2002. *J Am Soc Nephrol* 2006; 17:1143–1150.
21. Xue JL, et al. Incidence and mortality of acute renal failure in Medicare beneficiaries, 1992 to 2001. *J Am Soc Nephrol* 2006; 17:1135–1142.
22. Bagshaw SM, George C, Bellomo R. Changes in the incidence and outcome for early acute kidney injury in a cohort of Australian intensive care units. *Crit Care* 2007; 11:R68.
23. Ricci Z, Cruz D, Ronco C. The RIFLE criteria and mortality in acute kidney injury: A systematic review. *Kidney Int* 2008; 73:538–546.
24. Mehta RL, et al. Refining predictive models in critically ill patients with acute renal failure. *J Am Soc Nephrol* 2002; 13:1350–1357.
25. Lins RL, et al. Re-evaluation and modification of the Stuivenberg Hospital Acute Renal Failure (SHARF) scoring system for the prognosis of acute renal failure: an independent multicentre, prospective study. *Nephrol Dial Transplant* 2004; 19:2282–2288.
26. Uchino S, et al. Acute renal failure in critically ill patients: a multinational, multicenter study. *JAMA* 2005; 294:813–818.
27. Chertow GM, et al. Mortality after acute renal failure: models for prognostic stratification and risk adjustment. *Kidney Int* 2006; 70:1120–1126.
28. Schmitt R, et al. Recovery of kidney function after acute kidney injury in the elderly: a systematic review and meta-analysis. *Am J Kidney Dis* 2008; 52:262–271.
29. Ishani A, et al. Acute kidney injury increases risk of ESRD among elderly. *J Am Soc Nephrol* 2009; 20:223–228.
30. Lo LJ, et al. Dialysis-requiring acute renal failure increases the risk of progressive chronic kidney disease. *Kidney Int* 2009; 76:893–899.
31. Newsome BB, et al. Long-term risk of mortality and end-stage renal disease among the elderly after small increases in serum creatinine level during hospitalization for acute myocardial infarction. *Arch Intern Med* 2008; 168:609–616.
32. Schmitt R, Marlier A, Cantley LG. Zag expression during aging suppresses proliferation after kidney injury. *J Am Soc Nephrol* 2008; 19:2375–2383.
33. Wald R, et al. Chronic dialysis and death among survivors of acute kidney injury requiring dialysis. *JAMA* 2009; 302:1179–1185.
34. James MT, et al. Acute kidney injury following coronary angiography is associated with a long-term decline in kidney function. *Kidney Int* 2010; 78:803–809.
35. Wunsch H, et al. Three-year outcomes for Medicare beneficiaries who survive intensive care. *JAMA* 2010; 303:849–856.
36. Hsu CY. Where is the epidemic in kidney disease? *J Am Soc Nephrol* 2010; 21:1607–1611.


*Steven Coca, DO, is affiliated with the division of nephrology at Yale University. Mitchell Rosner, MD, is affiliated with the division of nephrology at the University of Virginia.*

# Chronic Kidney Disease in the Elderly

By Vanita Jassal

Chronic kidney disease (CKD) is likely to be the most common condition managed by practicing nephrologists in elderly patients attending a nephrology clinic. Why? Because the majority of individuals with renal disease are 65 or older (Figure 1) and CKD is the most common renal disease in the older individual.

Although it is a common condition, and each one of us is clearly able to manage CKD, many would argue that CKD should be considered a different disease for older individuals compared with younger people. The disorders and other causes for most cases of CKD are different in younger individuals, the health implications differ, and, at least in some respects, the appropriate treatment is age-sensitive.

Despite having a common final pathway, CKD in elderly individuals is more likely to result from chronic, asymptomatic conditions such as vascular disease, hypertension, obstructive uropathy, or repeated acute kidney injury than from inflammatory or systemic renal diseases. Consequently, the clinical presentation may differ, the management may be multidimensional, and the outcomes may be more dependent on comorbid illnesses.

At a population level, multiple studies have clearly shown that the presence of CKD is associated with increased mortality (in particular cardiac mortality), prolonged hospitalizations, and poorer long-term health outcomes (such as need for renal replacement therapy, myocardial infarction, strokes, etc,) across all age groups. However, a significant number of studies also emphasize that the relative increase in risk is considerably lower for elderly individuals than their younger counterparts. The implication is often that the presence of CKD is of lesser significance in older individuals than in younger individuals, but in fact, particularly when limited to those with a rapid decline in renal function (defined as those with a fall in eGFR of ≥ 3mL/min/yr), the increase in absolute risk of mortality is impressive.

The older individual is at higher baseline risk of one or more adverse health outcomes (death, ill-health, hospitalization) and so even small increases in relative risk result in dramatic increases in absolute risk. For example, a person of 40 years with an estimated glomerular filtration rate (eGFR) of 30–39 mL/min has an absolute increase in annual mortality of 2.2 percent compared to someone with normal renal function, while for the 75-year-old the absolute increase in mortality is almost double at 4.2 percent each year.

Screening and diagnosis of CKD is also more challenging in elderly populations. Isolated, or even multiple reports of low eGFR need to be interpreted in the context of a complete medical and, if possible, geriatric assessment. Comprehensive geriatric assessments (CGA) may help early recognition of frailty, muscle loss, and psychosocial factors, all of which may be associated with decreased muscle mass and overall well-being. Although time consuming, incorporation of periodic comprehensive geriatric assessments into routine CKD care also helps determine the most appropriate care path as CKD advances. A variety of widely available tools are available online for both physicians and other allied health staff (*http://www.healthcare.uiowa.edu/igec/resources-educators-professionals/*).

All equations that estimate renal function from measured serum creatinine values include age as a key modifying variable. The most commonly used, the abbreviated 4-item Modification of Diet in Renal Disease study (MDRD eGFR) equation, uses age as a surrogate for change in body composition.

The assumption (which works well at a population level) is that as one ages, one has a gradual fall in body muscle content. However at the individual level this relationship may not hold true. The age at which muscle loss starts, and the rate of loss, varies considerably between individuals. Nonmedical factors such as financial independence, access to food, and ability to prepare food, influence overall health.

Individuals who are fortunate and can maintain their health, independence, and exercise level, often have a slow, somewhat predictable decline in muscle mass with age. In these individuals the use of the MDRD formula will likely underestimate renal function. On the other hand, individuals who are dependent on caregivers to buy or prepare food, have cognitive issues, or medical conditions predisposing to frailty or prefrailty characteristics such as weight loss or reduced exercise tolerance are likely to have already experienced a significant degree of muscle loss at an early stage of life. These individuals are more likely to have 'normal' or low serum creatinine levels and therefore run the risk of unrecognized CKD.

Both overdiagnosis and underrecognition of CKD are of considerable concern. In the former situation, the simple act of labeling an otherwise healthy individual as one with CKD is likely to lead to unnecessary additional testing and follow-up, medications, and possibly impact quality of life. On the other hand, underrecognition of CKD may lead to errors in drug dosing and possible inappropriate prescribing of nonsteroidal drugs or radiological contrast. Although initial excitement over alternative creatinine-based formulae or measures such as cystatin C has waned, the search for the perfect "renal troponin" continues. Currently, the most optimal seems to be ongoing follow-p and evaluation for proteinuria, with eGFR estimation, and/or cystatin C measurement.

One of the most important clinical differences between elderly individuals and younger patients with CKD relates to treatment planning and therapeutic targets. The CGA is again a valuable tool in identifying possible detriments of the treatments traditionally used in CKD patients. CKD patients have higher levels of frailty, functional dependency and cognitive dysfunction and therefore are at higher risk of experiencing geriatric syndromes. Current blood pressure targets (≤130/80) offer little survival benefit for older patients and, particularly in those with reduced mobility or a tendency to fall, emphasis must be placed not only on the absolute sitting blood pressure but also on postural changes.

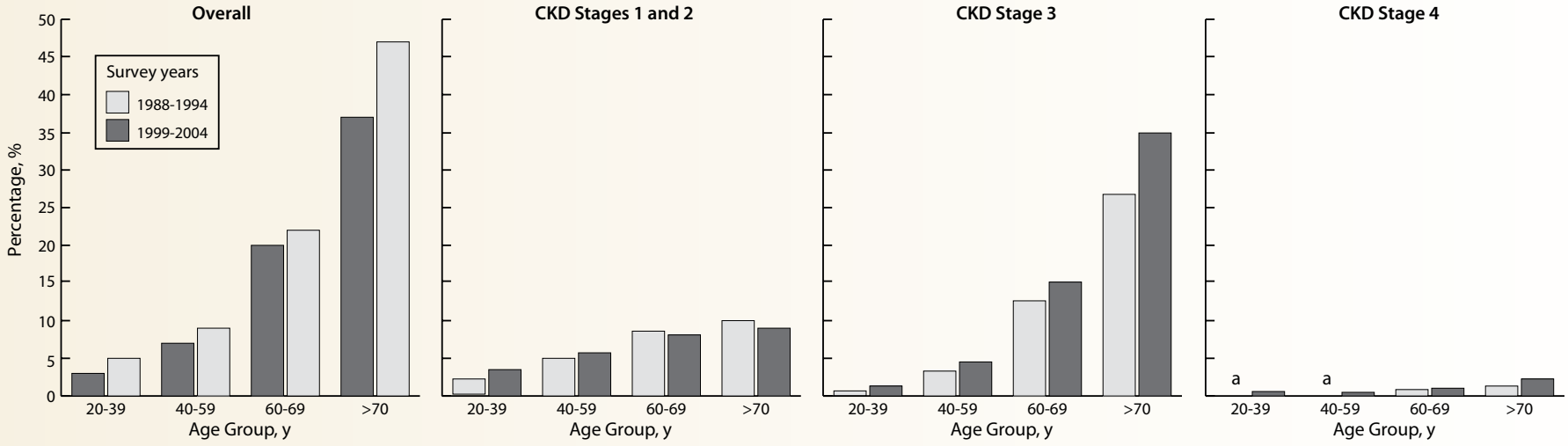
Recognition of the financial circumstances of an older patient may influence drug prescribing, while environmental assessments may influence dialysis modality choices and/or nursing strategies.

In the advanced stages of CKD, patients and families are often educated about different renal replacement strategies. The CGA is again a useful tool at this point. Documentation of changes over time, noted on sequential evaluations, may help families and patients appreciate subtle but significant changes in their nonrenal health and help during discussions about dialysis and nondialysis care strategies, dialysis withdrawal, and advanced planning.

Barriers to home dialysis may be recognized and overcome early in the dialysis planning period. Discussions around fistula creation may be guided by CGA evaluation findings. Current

*Continued on page 12*

**Figure 1. Prevalence of CKD in NHANES 1988—1994 and 1999–2004 by age group (reprinted from *JAMA*, 2007)**




NHANES indicates National Health and Nutrition Examination Surveys.
[a]There were no cases in 1988-1994.

## CKD in the Elderly

*Continued from page 11*

guidelines suggesting preemptive fistula creation in patients planning for hemodialysis do not differentiate between the 40-year-old and 80-year-old patient with stage 4/5 CKD. However, older patients are at higher than normal risk of fistula failure-to-mature; death prior to dialysis-need; and only have modest survival rates after dialysis initiation.

In the recently published ASN geriatric nephrology curriculum Seth Wright and John Danzinger discuss in detail the benefits, and risks, of fistula creation and advocate caution and careful consideration prior to referral for surgery. One option is to consider delaying fistula creation for three to six months while the older patient is established onto dialysis and adjusts to their new lifestyle.

The use of the CGA helps clinicians appreciate that the detection and management of CKD in elderly individuals requires ongoing collaboration with allied health and palliative care teams, geriatricians, as well as the family and patient. An appreciation of the impact that renal disease has on diet, lifestyle and well-being is necessary. To this point, it is humbling and insightful to take a few minutes to hear the patient's perspective (http://www.youtube.com/watch?v=EOciMaCyJW4).

**Suggested reading**


1. American Society of Nephrology Geriatric Nephrology Curriculum http://www.asn-online.org/education_and_meetings/geriatrics/ accessed 31 Dec 2010.
2. NephSAP 2011, volume 10 Geriatric Nephrology, January 2011.
3. Coresh J, Selvin E, Stevens LA, et al. Prevalence of chronic kidney disease in the United States. *J Am Med Assoc* 2007; 298:2038–2047.
4. Shlipak MG, Katz R, B. Kestenbaum, et al. Rapid decline of kidney function increases cardiovascular risk in the elderly. *J Am Soc Nephrol* 2009.
5. Anderson S, Halter JB, Hazzard WR, et al. Prediction, progression, and outcomes of chronic kidney disease in older adults. *J Am Soc Nephrol* 2009; 20:1199–1209.
6. S. V. Jassal and D. Watson. Doc, don't procrastinate...Rehabilitate, palliate, and advocate. *Am J Kidney Dis.* 2010; 55:209-212, 2010.


*Vanita Jassal is a staff nephrologist at the University Health Network and associate professor at the University of Toronto.*

# Special Considerations for Dialysis in the Elderly

By Yi-Wen Chiu and Rajnish Mehrotra

In the United States, as in many other developed countries, the incidence of treated end stage renal disease (ESRD) increases with advancing age; the highest rates are observed in individuals between the ages of 75 and 79 (Figure 1) (1). There is concern, however, that the functional rehabilitation of elderly dialysis patients is often unsatisfactory and the gain in life expectancy with renal replacement therapy is rather modest. This should not be surprising, because elderly patients with ESRD have a significantly greater burden of coexisting illnesses and are more likely to be frail.

Unique psychosocial issues that interplay with medical conditions must be factored in when planning for renal replacement therapy for the elderly. Consequently, nephrologists grapple with several important issues when dealing with an elderly patient with advanced chronic kidney disease (CKD): Is dialysis planning appropriate for all elderly CKD patients? Does dialysis therapy improve the functional status and increase the life expectancy of the frail elderly, and is there a role for maximum conservative therapy? Does dialysis increase the risk of death in elderly patients if started at a higher level of estimated glomerular filtration rate (eGFR)? Is one dialysis modality better than the other for elderly patients with ESRD?

### Dialysis planning for the elderly: for whom, and when?

One of the areas in the field of nephrology with the greatest opportunity to improve the management of patients is the time of dialysis initiation. To improve the early outcomes of ESRD patients, it is often recommended that dialysis planning begin when the eGFR decreases to <30 mL/min/1.73 $m^2$. However, several epidemiologic studies from unselected populations have shown that in patients with advanced CKD, the risk for death is higher than the future need for dialysis; this is the case for the elderly, in particular (2). Therefore, dialysis planning can be futile if it is to begin for every elderly patient with eGFR <30 mL/min/1.73 $m^2$.

Recent studies suggest that individuals with significant proteinuria, or an underlying primary renal disease, or with declining trajectory of renal function are more likely to need dialysis. If these issues, along with the patient's functional status, are factored in when deciding which elderly patients with low eGFR should begin preparing for dialysis, the potential futility of the process could be reduced.

### A role for maximum conservative management?

The life expectancy of patients starting dialysis therapy in the United States is about one-quarter of age- and sex-matched individuals without kidney disease, and elderly patients starting dialysis are no exception (1). The median life expectancy of dialysis patients between the ages of 75 and 79 is 2.9 years, compared with 10.8 years for individuals in the general population (3).

A recent study has focused on the dismal outcomes of frail elderly nursing home residents. An overwhelming majority of such patients experienced continued functional decline and/or death within 12 months of starting dialysis (4). Studies such as this suggest that in frail individuals with advanced CKD, starting dialysis may not necessarily improve their functional status and/or increase their life expectancy. These observations have also spurred interest in considering maximum conservative care as one of the therapeutic options for frail elderly patients with advanced CKD in lieu of preparation for dialysis, including anemia correction with erythropoietin, loop diuretics to prevent volume overload, phosphate-binders to manage itching, and potassium restriction as the only dietary intervention (5).

Choosing between maximum conservative management and renal replacement therapy requires shared decision-making that should involve the nephrologist, the patient, and the patient's family. A time-limited trial of dialysis may facilitate decision-making for some patients. Patients who choose maximum conservative management or withdraw from dialysis after a time-limited trial may also be appropriate candidates for hospice care at some stage of their disease.

### What is the optimal time to begin dialysis therapy?

In the United States, patients are starting dialysis therapy at progressively higher levels of eGFR; the higher the age, the greater the proportion of individuals who begin dialysis at an eGFR >10 mL/min/1.73 $m^2$ (1, 6). Several observational studies have shown an inverse relationship between eGFR at the start of renal replacement therapy and the subsequent risk for death, leading some to argue that it is the dialysis treatment itself that is at least partly responsible for the higher mortality in patients who start dialysis early (7). However, the same studies indicate that patients who begin dialysis at higher levels of eGFR are much more likely to be men, elderly, diabetic, and with greater cardiovascular comorbidity (7).

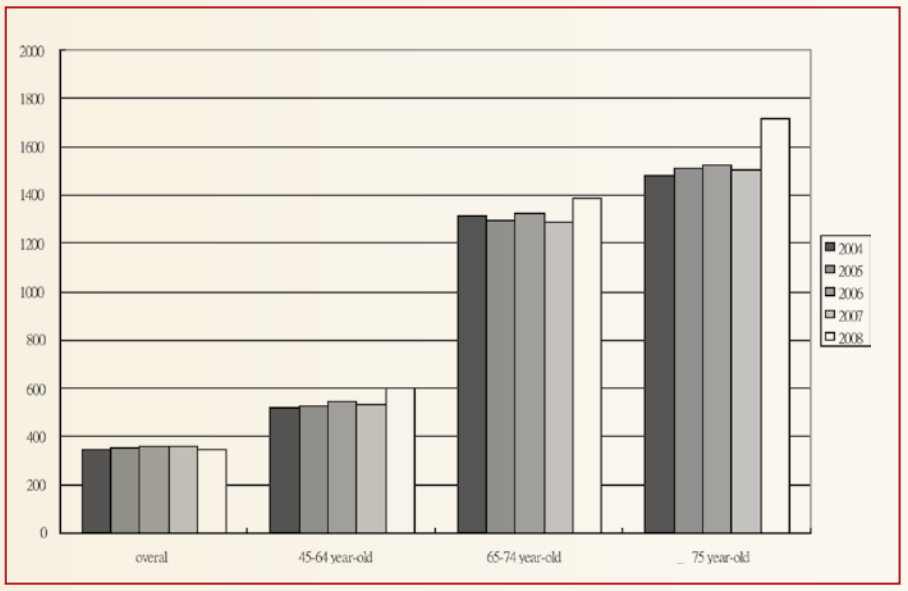
Given the lack of detail about the clinical status of individual patients in national registries such as the U.S. Renal Data System, it is unlikely that statistical adjustments will account for the greater disease burden of patients who begin dialysis at higher levels of renal function. Furthermore, the results of the recently published IDEAL study indicate that starting dialysis at higher levels of eGFR does not itself increase the risk for death (8). These considerations suggest that in symptomatic individuals, it is safe to start dialysis even if the eGFR is >10 mL/min/1.73 $m^2$. Conversely, dialysis may be safely withheld in otherwise asymptomatic individuals with lower eGFR. However, the results of the IDEAL study suggest that many elderly CKD patients with declining renal function are likely to require dialysis at higher levels of renal function (8).

### Is one dialysis modality better than the other for elderly patients with ESRD?

The overwhelming majority of ESRD patients in the United States are treated with in-center hemodialysis; peritoneal dialysis remains the dominant home dialysis modality (1). Numerous observational studies have compared the outcomes of patients treated with in-center hemodialysis and peritoneal dialysis. These studies suggest that elderly patients treated with peritoneal dialysis, particularly those with diabetes mellitus and/or coexisting illnesses, have a somewhat shorter survival than those treated with in-center hemodialysis (9). However, over the past decade in the United States, improvements in the outcomes of peritoneal dialysis patients have outpaced those seen with in-center hemodialysis patients (10). Thus, in the most recent cohorts, the differences in survival seen in patients treated with either dialysis modality have substantially narrowed and are probably not clinical meaningful (11).

These findings suggest that the survival studies should have little if any bearing when assisting elderly patients and/or their families in selecting an appropriate dialysis modality. On one hand, the burden of coexisting diseases, frailty, and social isolation may make in-center hemodialysis a particularly attractive therapeutic option for many elderly ESRD patients. On the other hand, the ability to undergo dialysis at home may be perceived by some elderly patients as the best method for them to maintain their independence and dignity. Peritoneal dialysis has been successfully performed by octogenarians and nonagenarians, and this

**Figure 1. Incidence of treated end stage renal disease in the United States**




may be further facilitated by identifying family members or other support services that may provide assistance to patients to undergo home dialysis (12). Success of this concept of assisted home peritoneal dialysis has been reported from Canada, Denmark, and France, and should be considered for appropriate individuals. It follows, then, that the best dialysis modality for a patient is the one that best fits into their lifestyle and their expectations and goals for their care. Hence, all patients and/or their families should be offered the choice of all dialysis modalities whenever feasible under the oversight and encouragement offered by the health care team.

In conclusion, there are many unique challenges in the care of elderly ESRD patients. These challenges begin from the time of preparation for dialysis therapy to initiation and subsequently the maintenance of dialysis therapy. It is important to focus not only on longevity but also on quality of life and quality of death.

*Yi-Wen Chiu is affiliated with Kaohsiung Medical University. Rajnish Mehrotra is affiliated with Los Angeles Biomedical Research Institute at Harbor-UCLA and David Geffen School of Medicine at UCLA. Rajnish Mehrotra has received grant support and honoraria from Baxter Health Care.*

**References**

1. US Renal Data System. *UADRAoCK-DaE-SRDitUS*, Bethesda, MD, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, 2010.
2. Keith DS, et al. Longitudinal follow-up and outcomes among a population with chronic kidney disease in a large managed care organization. *Arch Intern Med* 2004; 164:659–663.
3. US Renal Data System. *UADRAoCK-DaE-SRDitUS*, Bethesda, MD, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, 2009.
4. Kurella Tamura M, et al. Functional status of elderly adults before and after initiation of dialysis. *N Engl J Med* 2009; 361:1539–1547.
5. Carson RC, et al. Is maximum conservative management an equivalent treatment option to dialysis for elderly patients with significant comorbid disease? *Clin J Am Soc Nephrol* 2009; 4:1611–1619.
6. Rosansky SJ, et al. Initiation of dialysis at higher GFRs: is the apparent rising tide of early dialysis harmful or helpful? *Kidney Int* 2009; 76:257–261.
7. Kazmi WH, et al. Effect of comorbidity on the increased mortality associated with early initiation of dialysis. *Am J Kidney Dis* 2005; 46:887–896.
8. Cooper BA, et al. A randomized, controlled trial of early versus late initiation of dialysis. *N Engl J Med* 2010; 363:609–619.
9. Jiwakanon S, et al. Peritoneal dialysis: an underutilized modality. *Curr Opin Nephrol Hypertens* 2010; 19:573–577.
10. Mehrotra R, et al. Chronic peritoneal dialysis in the United States: declining utilization despite improving outcomes. *J Am Soc Nephrol* 2007; 18:2781–2788.
11. Mehrotra R, et al. Similar outcomes with hemodialysis and peritoneal dialysis in patients with end-stage renal disease. *Arch Intern Med* 2010.
12. Dimkovic NB, et al. Chronic peritoneal dialysis in octogenarians. *Nephrol Dial Transplant* 2001; 16:2034–2040.

# Hypertension in the Elderly: Two Decades Later, What Have We Learned Since the SHEP Trial?

By Madhav Rao and George Bakris

Hypertension is common in people 60 and older. With increasing age, it is more likely that someone will experience hypertension and die of coronary heart disease even in the prehypertension range (1, 2) (Figure 1). According to the National Health and Nutrition Examination Survey (NHANES) 1999 to 2006, approximately 67 percent of adults in the United States 60 and older had hypertension, a 10 percent increase from NHANES 1988 to 2004 (3). African Americans and women had a higher prevalence of hypertension than did white individuals, and in those 70 and older the hypertension was more poorly controlled than in those 60–69 (3) (Figure 2).

## Definition and significance of hypertension

The Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC 7) defines stage 1 hypertension as a systolic BP ≥140 mm Hg or a diastolic BP ≥90 mm Hg (4). Isolated systolic hypertension is a systolic BP ≥140 mm Hg but a diastolic BP of ≤90 mm Hg. It affects about two thirds of individuals above age 60 and approximately 75 percent of those over age 75. Among older individuals, systolic BP is a stronger predictor of cardiovascular disease events and end stage renal disease (5).

## Aging and pathophysiology of hypertension

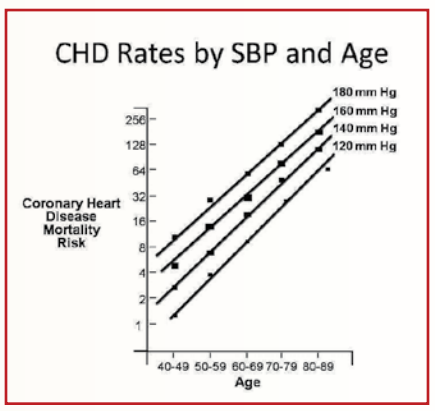
Aging is associated with a reduction in arterial compliance, primarily affecting the aorta and other large blood vessels. Alterations of various collagens in the vessel wall decrease elasticity and increase fibrosis and sclerosis of the blood vessels. As a result, arterial stiffness increases, and distensibility of the larger arteries decreases, resulting in widened pulse pressure. The Framingham Heart Study suggested that both systolic and diastolic BP increase in parallel until the age of 50. Thereafter, systolic BP continues to rise and diastolic BP drops, resulting in a widened pulse pressure (6).

Salt sensitivity is defined as an increase in systolic pressure of >10 mm Hg over a few hours after the intake of a fixed amount of salt. Salt sensitivity plays an important role in the pathophysiology of hypertension in the elderly. Older individuals are relatively more salt sensitive than are people under age 50 because of a variety of factors, including reduced nitric oxide from the endothelium in response to various stimuli, loss of integrity of various collagen subfractions, and altered handling of sodium by the kidney. Some contributing factors in the kidney include reduced generation of prostaglandins and dopamine in response to vasoconstrictor stimuli, and increased oxidant stress directly mediated by high sodium intake (7, 8). Age-associated decline in the activity of membrane sodium/potassium–ATPase may increase intracellular sodium and reduce sodium–calcium exchange. This increases intracellular calcium and vascular resistance. Reductions in cellular calcium efflux due to reduced calcium–ATPase activity may have a similar effect (9).

## BP goal in the elderly

The JNC 7 guidelines suggest a goal BP of <140/90 mm Hg in all patients, including the elderly. However, we have learned from the Systolic Hypertension in Elderly Program (SHEP) that among patients with isolated systemic hypertension, reduction of diastolic BP below 60–65 mm Hg after the initiation of antihypertensive therapy is associated with higher cardiovascular event rates. Since the SHEP, several retrospective studies have supported this contention (10–12). The results of these analyses suggest that optimal reduction in diastolic BP in the elderly should not exceed 60–65 mm Hg during attempts to reduce the systolic BP below 140 mm Hg. The key exception to this recommendation is a history of angina; patients so affected should maintain a diastolic pressure >80 mm Hg.

**Figure 1. Coronary heart disease risk in the context of age and level of BP. Data adapted from Lewington et al. (1) and Weber (2).**

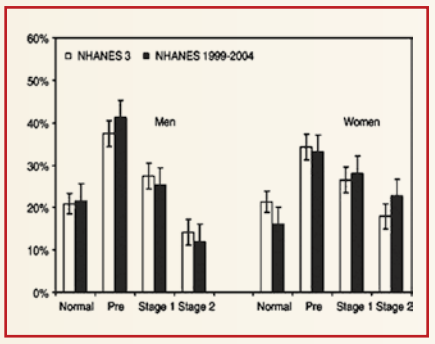



*Continued on page 14*

# Hypertension in the Elderly

*Continued from page 13*

**Figure 2. Age-adjusted and age-specific prevalence distribution and 95 percent confidence intervals (CIs) for BP classification groups according to the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure, United States population aged 60 and older, National Health and Nutrition Examination Survey 1988–2004. Data adapted from Ostchega et al. (3).**




### *Approach to hypertension in an elderly patient*

Lifestyle modifications such as weight reduction and restriction of salt intake to <3 g/day reduce BP effectively. Elderly individuals tend to ingest increasing amounts of salt because of their diminished taste sensitivity (13).

The efficacy of weight reduction and salt restriction in elderly patients was studied in the Trial of Nonpharmacological Interventions in the Elderly (TONE) (14). In TONE, 975 patients aged 60 to 80 years with a BP below 145/85 mm Hg while receiving treatment with a single antihypertensive medication were each randomized to one of four groups: salt restriction, weight reduction, both salt restriction and weight reduction, and usual care. The primary endpoint was an elevated BP at one or more study visits after withdrawal of antihypertensive medication, need for continual treatment with antihypertensive medication, or a cardiovascular event. Of those who restricted their salt intake, 38 percent did not achieve the primary endpoint in comparison with 24 percent in the usual care group. In the weight loss group, 39 percent remained free of primary endpoints in comparison with 26 percent. In the weight loss and salt restriction group, the results were even better: 44 percent versus 16 percent did not have an increase in BP (14). In this study, the goal of sodium restriction was 1.8 g/24 hours (approximately ⅔ teaspoon/day), and the goal for weight reduction was 10 pounds.

Elderly patients are more likely than younger individuals to take nonsteroidal anti-inflammatory drugs (NSAIDS) for arthritis pain. NSAIDS cause edema and hypertension by inhibiting the production of vasodilatory prostaglandins (15). The use of NSAIDS increases BP as much as 6 mm Hg (16). Furthermore, NSAIDS can interfere with the antihypertensive effects of all agents except calcium antagonists. Therefore, they should be used sparingly in the elderly hypertensive population (17).

### *Pharmacologic treatment*

The Blood Pressure Treatment Trialists Collaboration, a meta-analysis of 31 trials involving 190,606 patients with a mean age of 65 years, concluded that all classes of antihypertensive agents were equally successful in reducing the risk of cardiovascular events (18). The reduction in risk was directly proportional to the reduction in the systolic BP. More recently, the benefits of lower BP in patients over age 80 were demonstrated in the Hypertension in the VERY Elderly Trial (20). In this study, 3845 patients 80 or older who had a systolic BP of ≥160 mm Hg were randomized to indapamide or placebo. The angiotensin-converting enzyme inhibitor perindopril or matching placebo was added to achieve a BP of 150/80 mm Hg if necessary. The primary endpoint was fatal or nonfatal stroke. After two years, the treatment group showed a 30 percent reduction in stroke, a 21 percent reduction in death, a 23 percent reduction in cardiovascular death, and a 64 percent reduction in heart failure (20). These results support the use of antihypertensive medications in patients above 80 years of age.

### *Choice of antihypertensive medication*

Various treatment guidelines note that the selection of antihypertensive agents should be based on the presence or absence of concurrent medical conditions. Since the SHEP, several studies in the elderly have yielded the following observations, which are consistent in all trials. First, as single agents, calcium antagonists and thiazide-type diuretics provide the greatest relative reductions in BP compared with other classes. Second, all trials in the elderly clearly show that two or more agents are needed to achieve BP goals, i.e., a systolic pressure of <140 mm Hg or at least <160 mm Hg in patients with very poor vascular compliance (21–23). Note that two-drug combination therapy should be given to patients whose BP is more than 20/10 mm Hg above their respective goals. Third, it appears that a blocker of the renin–angiotensin system may provide a greater benefit to cardiovascular and renal risk reduction than a diuretic; this is supported by data from ACCOMPLISH, an outcome trial in 11,506 people with a mean age of 68 years (23, 24). Last, initial doses of antihypertensive agents in elderly patients should be low because these patients are more prone to orthostatic hypotension, dehydration, and electrolyte imbalances. Patients should be closely monitored for symptoms and side effects, and electrolyte levels and kidney function should be monitored every few months.

**References**


1. Lewington S, et al. Age-specific relevance of usual blood pressure to vascular mortality: A meta-analysis of individual data for one million adults in 61 prospective studies. *Lancet* 2002; 360:1903–1913.
2. Weber MA. Exploring a new definition of hypertension. *Rev Cardiovasc Med* 2005; 6:164–172.
3. Ostchega Y, et al. Trends in hypertension prevalence, awareness, treatment, and control in older U.S. adults: Data from the National Health and Nutrition Examination Survey 1988 to 2004. *J Am Geriatr Soc* 2007; 55:1056–1065.
4. Chobanian AV, et al. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: The JNC 7 report. *JAMA* 2003; 289:2560–2572.
5. Benetos A, et al. Prognostic value of systolic and diastolic blood pressure in treated hypertensive men. *Arch Intern Med* 2002; 162:577–581.
6. Franklin SS, et al. Hemodynamic patterns of age-related changes in blood pressure: The Framingham Heart Study. *Circulation* 1997; 96:308–315.
7. Phillips PA, et al. Neuroendocrine mechanisms and cardiovascular homeostasis in the elderly. *Cardiovasc Drugs Ther* 1991; 4[Suppl 6]:1209–1213.
8. Campese VM. Salt sensitivity in hypertension: Renal and cardiovascular implications. *Hypertension* 1994; 23:531–550.
9. Zemel MB, Sowers JR. Salt sensitivity and systemic hypertension in the elderly. *Am J Cardiol* 1988; 61:7H–12H.
10. Messerli FH, Kupfer S, Pepine CJ. J curve in hypertension and coronary artery disease. *Am J Cardiol* 2005; 95:160.
11. Prevention of stroke by antihypertensive drug treatment in older persons with isolated systolic hypertension. Final results of the Systolic Hypertension in the Elderly Program (SHEP). SHEP Cooperative Research Group. *JAMA* 1991; 265:3255–3264.
12. Messerli FH, et al. Dogma disputed: Can aggressively lowering blood pressure in hypertensive patients with coronary artery disease be dangerous? *Ann Intern Med* 2006; 144:884–893.
13. Stevens JC. Detection of tastes in mixture with other tastes: Issues of masking and aging. *Chem Senses* 1996; 21:211–221.
14. Whelton PK, et al. Sodium reduction and weight loss in the treatment of hypertension in older persons: A randomized controlled trial of nonpharmacologic interventions in the elderly (TONE). TONE Collaborative Research Group. *JAMA* 1998; 279:839–846.
15. de Leeuw PW. Nonsteroidal antiinflammatory drugs and hypertension: The risks in perspective. *Drugs* 1996; 51:179–187.
16. Johnson AG. NSAIDs and increased blood pressure: What is the clinical significance? *Drug Saf* 1997; 17:277–289.
17. Whelton A, et al. Effects of celecoxib and naproxen on renal function in the elderly. *Arch Intern Med* 2000; 160:1465–1470.
18. Turnbull F, et al. Effects of different regimens to lower blood pressure on major cardiovascular events in older and younger adults: Meta-analysis of randomised trials. *BMJ* 2008; 336:1121–1123.
19. Perry HM, Jr., et al. Effect of treating isolated systolic hypertension on the risk of developing various types and subtypes of stroke: The Systolic Hypertension in the Elderly Program (SHEP). *JAMA* 2000; 284:465–471.
20. Beckett NS, et al. Treatment of hypertension in patients 80 years of age or older. *N Engl J Med* 2008; 358:1887–1898.
21. Major outcomes in high-risk hypertensive patients randomized to angiotensin-converting enzyme inhibitor or calcium channel blocker vs diuretic: The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). *JAMA* 2002; 288:2981–2997.
22. Wing LM, et al. A comparison of outcomes with angiotensin-converting–enzyme inhibitors and diuretics for hypertension in the elderly. *N Engl J Med* 2003; 348:583–592.
23. Jamerson K, et al. Benazepril plus amlodipine or hydrochlorothiazide for hypertension in high-risk patients. *N Engl J Med* 2008; 359:2417–2428.
24. Bakris GL, et al. Renal outcomes with different fixed-dose combination therapies in patients with hypertension at high risk for cardiovascular events (ACCOMPLISH): A prespecified secondary analysis of a randomised controlled trial. *Lancet* 2010; 375:1173–1181.


*Madhav Rao, MD, is affiliated with Associates in Nephrology in Chicago, and George Bakris, MD, FASN, is affiliated with the Department of Medicine, Hypertensive Diseases Unit, University of Chicago Pritzker School of Medicine.*

# Kidney Transplantation in the Elderly: It's Not All Gloom and Doom

By Viresh Mohanlal and Matthew R.Weir

In the United States, the number of end stage renal disease (ESRD) patients on maintenance dialysis has increased 20 percent in the last decade to 1700 per million, and 100,000 new cases are added every year. The largest increase in both incident and prevalent cases of ESRD has been in individuals ≥65, with rates three- to fourfold higher compared with younger individuals (Figure 1). Nearly 50 percent of all patients on dialysis are ≥65. This increase in the older patient population is likely due to the increasing prevalence of diabetes and hypertension that has contributed to a rise in ESRD. In addition, the average life expectancy of patients on dialysis has improved in the last two decades. Nevertheless, the rate of death is six times higher for patients on dialysis compared with the general population, with mortality being highest in the elderly population (1).

## Do elderly patients benefit from kidney transplantation?

Although the rate of kidney transplantation among older patients is 5 to 15 times lower than that among patients ≤65, this rate has increased by 54 percent in the last decade (2). This increase indicates that kidney transplantation offers better survival and quality of life, even among elderly patients. Most of the earlier studies showing survival benefit among patients undergoing kidney transplantation were criticized for including healthy patients in large cohorts of dialysis patients. This selection bias was overcome in a large U.S. study involving 228,552 dialysis patients in whom outcomes were compared only between patients on the waiting list for kidney transplantation and patients who received a kidney transplant (3). Of the 88,500 patients who were ≥60, only 6925 (8 percent) were wait-listed for transplantation, around half of whom eventually underwent deceased donor transplantation. On comparing outcomes among patients 60 to 70 and those who remained wait-listed on dialysis, the risk of death among transplanted patients was highest within the first two weeks and remained high until 148 days after transplantation. Long-term mortality risk was 61 percent lower among patients who underwent kidney transplantation. This translated into an average increase in life span of 4.3 and 2.8 years for patients 60 to 64 and 64 to 69 years of age, respectively. Similarly, in a Scandinavian study involving 325 patients 60 to 70, the 1-, 5-, and 7-year survival rates were 93, 70, and 46 percent in the transplanted group compared with 81, 30, and 15 percent in the wait-listed group, with an average increase in life expectancy of 3 years (4).

Rao et al. (5) performed a large retrospective analysis to determine outcomes in 5567 patients ≥70 who underwent kidney transplantation in the United States from 1990 to 2003. One in five patients was ≥75. Although the survival rate was equal among the transplanted and wait-listed patients in the first 2 years, the long-term mortality risk was 56 percent lower for kidney transplant recipients (Figure 2). At 4 years, the adjusted survival for transplant recipients was 66 percent compared with 51 percent in the wait-listed patients. This survival benefit was most notable in ESRD patients with diabetes and hypertension. Even elderly patients ≥75 had a 33 percent reduction in mortality after kidney transplantation. The 1- and 3-year graft survival rates among transplant recipients were 93.1 and 89.1 percent, respectively.

In a recent study of a highly selected group of patients with a median age of 81, death-censored graft survival was reported to be similar to that of patients 60 to 69 (6), although perioperative mortality was higher (2.5 percent versus 1.5 percent). Based on these data, it is obvious that there is no age limit for kidney transplantation. Carefully selected elderly patients clearly benefit from transplantation. In addition to the survival benefit and improved quality of life, kidney transplantation may be an economically viable option in older individuals, particularly if the waiting period is less than 2 years. Beyond this, the financial benefits tend to be variable. Live donor kidney transplantation is therefore an attractive option for these patients.

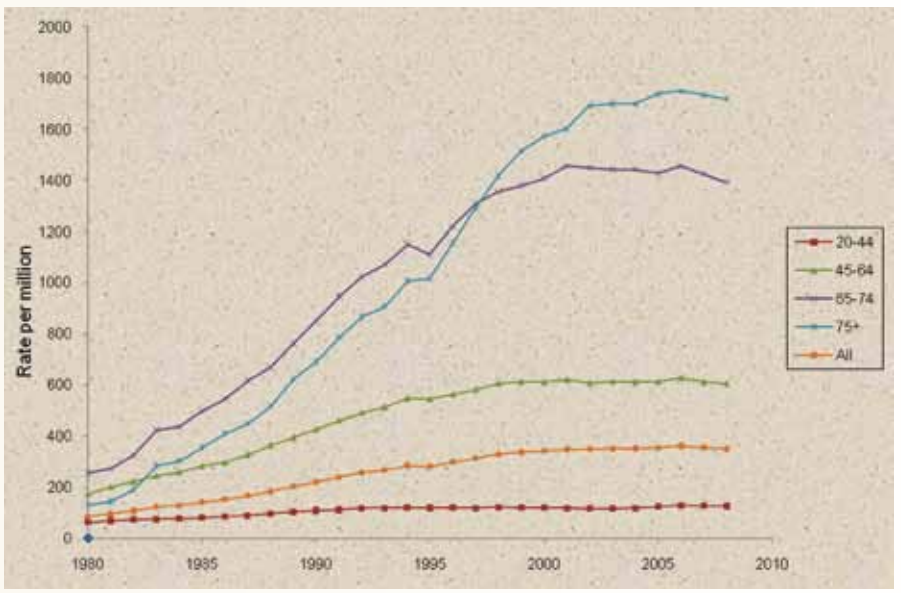
## How can we meet the growing demand for kidney transplantation in the elderly?

The benefits of transplantation noted in these studies have resulted in a growing demand for kidney transplantation in the elderly population, who now constitute the fastest growing segment of the waiting list population (Figure 3). Currently, one in six patients wait-listed for kidney transplantation is ≥65, and the waiting time has increased to 3.6 years in the last 2 years. It is projected that without transplantation, 46 percent of these patients are likely to die while on the waiting list (7).

The number of kidney transplantations performed annually has not matched this increasing demand, especially in the elderly population. This is largely due to organ shortage, a paucity of live donors, changes in organ allocation policies that favor young recipients, lack of referrals for transplantation evaluation due to physician attitudes toward the elderly, and ethical concerns about offering a kidney to an older patient versus a younger patient. It has been argued that although kidney transplantation offers improved survival in the elderly as opposed to remaining on dialysis, the magnitude of benefit is not the same as in younger groups. The average life expectancy increases by 11 years in patients 40 to 59 versus only 4 years in patients 60 to 70 in the absence of comorbidities such as vascular disease or diabetes. However, death-censored allograft survival is similar in older and younger patients and is independent of age. Therefore, it has been suggested that through preferential transplantation of organs from the older donor to the older recipient, overall graft survival may be optimized.

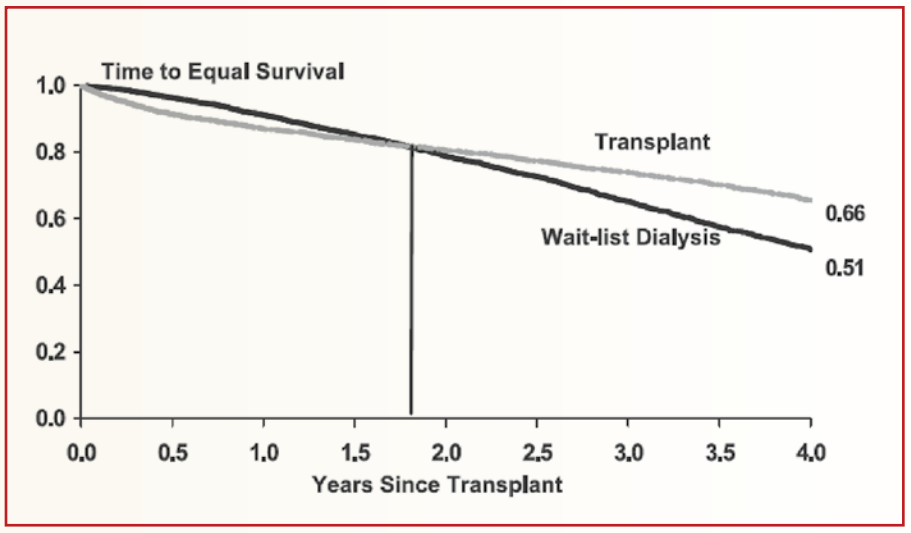
To meet this growing demand for kidney transplantation in the elderly and to overcome the organ shortage, several kidney transplant centers have used the strategy of increasing the donor pool by accepting expanded criteria kidneys, defined as donor age ≥60 or ≥50 with any two of the following conditions: history of hypertension, serum creatinine level ≥1.5 mg/dL, or death due to cerebrov-

**Figure 1. Incidence rate of ESRD by age categories in the United States (1980 to 2008)**




**Adapted from U.S. Renal Data System. *USRDS 2008 Annual Data Report: Atlas of Chronic Kidney Disease and End-Stage Renal Disease in the United States*, Bethesda, MD, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, 2008.**

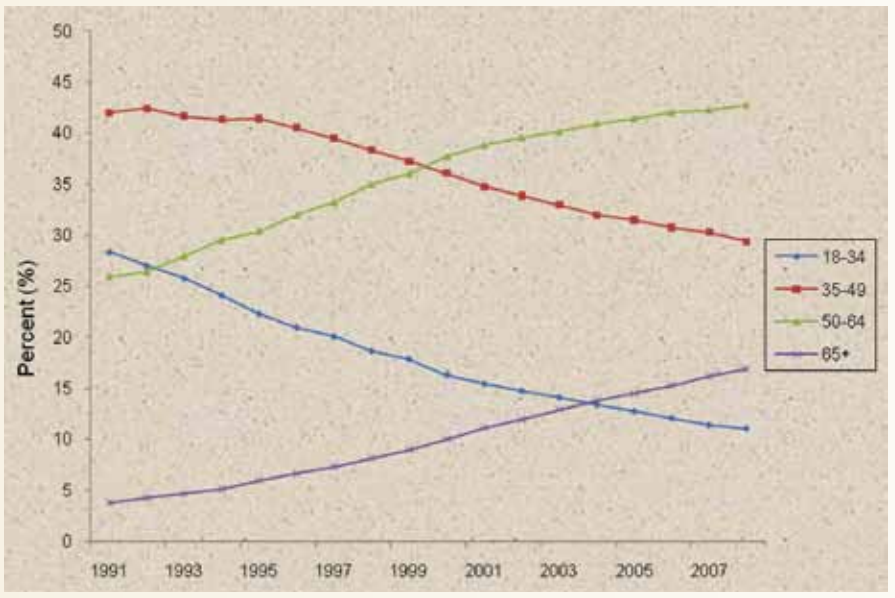
**Figure 2. Cumulative survival curves for elderly kidney transplant recipients who underwent kidney transplantation and those who remained wait-listed on dialysis**




**Reprinted with permission from Rao PS, et al. Renal transplantation in elderly patients older than 70 years of age: results from the Scientific Registry of Transplant Recipients. Transplantation 2007; 83:1069–1074.**

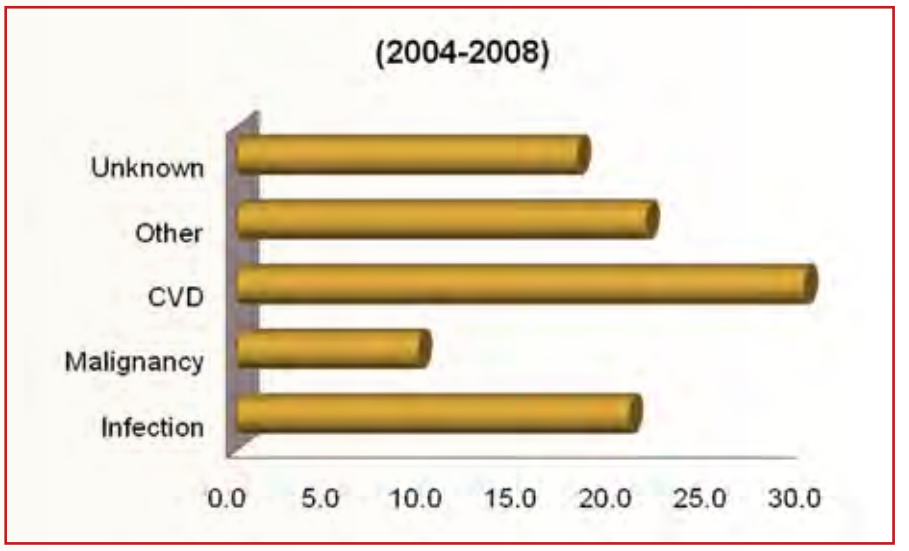
*Continued on page 16*

**Figure 3. Distribution of the wait-listed population by age (1991 to 2008)**




**Adapted from U.S. Renal Data System. *USRDS 2010 Annual Data Report: Atlas of Chronic Kidney Disease and End-Stage Renal Disease in the United States,* Bethesda, MD, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, 2010.**

**Figure 4. Causes of death with a functioning graft in adult kidney transplant recipients**




**Adapted from U.S. Renal Data System. *USRDS 2010 Annual Data Report: Atlas of Chronic Kidney Disease and End-Stage Renal Disease in the United States*, Bethesda, MD, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, 2010.**

ascular disease. Previously, ≥50 percent of these kidneys were discarded due to a higher risk of graft failure compared with standard criteria organs (8). The logical question posed is: Is it beneficial for an elderly patient to receive an expanded criteria kidney as opposed to remaining on dialysis? This question was answered in an elegant study by Ojo et al. (9). They demonstrated that although patients who received "marginal kidneys" (defined as age >55, cold ischemia time >36 hours, 10-year history of diabetes or hypertension, and donation after cardiac death kidney) had an adjusted 5-year survival of 59 percent compared with 72 percent among standard criteria kidney recipients ($p < 0.001$), the average life expectancy improved by 3.8 years in these patients as opposed to wait-listed dialysis patients.

Another strategy of increasing the donor pool to improving chances of transplantation in the elderly has been to offer an older donor kidney to the elderly recipient to optimize survival. This hypothesis was tested as a part of the European Senior Transplant Program in which 18 "very old" donor kidneys (mean age, 78) were transplanted into older individuals (mean age, 68 years) and compared with the two control groups who received age-matched kidneys (mean age, 68 for donor and recipient) and HLA-matched kidneys (mean age of donor, 48; mean age of recipient, 68), respectively (10). The 1-, 3-, and 5-year survival rates were 93, 83, and 80 percent, respectively, in the study group and did not differ significantly with the control group. In this study, however, the average cold ischemia time was ≤10 hours, a critical factor that favored good graft outcomes.

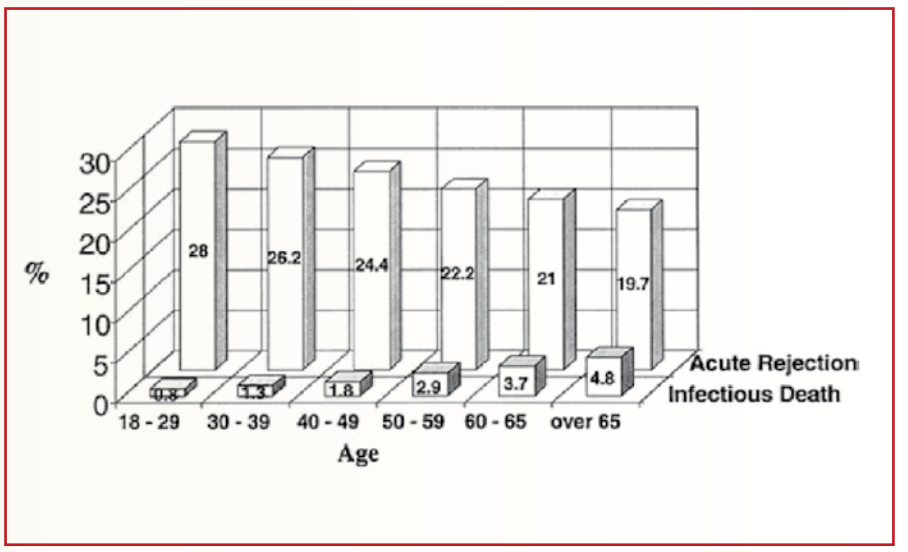
Recent studies have also reported favorable patient and graft survival outcomes with transplantation from old live donors compared with standard criteria donors and comparable outcomes with young live donors. This is encouraging news, because the addition of older live donors to the pool may help reduce the waiting times for transplantation, which is so crucial for survival in this elderly population. Transplanting two marginal kidneys instead of one and paired living donor match programs are also other options and have met with reasonable success at several transplant centers in the United States and abroad (11).

## How should we determine the suitability of the elderly patient for transplantation?

Patient selection is crucial, because not all elderly patients benefit from kidney transplantation. In the Minnesota study that examined the risk factors for graft loss among the elderly, the 10-year graft survival was 39 percent versus 53 percent among younger recipients. Although graft loss due to death was the predominant cause, the major risk factors identified were nonskin malignancies, vascular disease, smoking, and donor age (12). The risk of malignancy after transplantation was five times higher in elderly patients and inversely correlated with the time of remission of the cancer. Infection episodes were also fivefold higher, particularly with the presence of comorbidities such as diabetes, diverticulitis, and urinary tract infections. Cardiovascular disease, infectious complications, and malignancies account for most deaths in elderly patients after transplantation (Figure 4). It is therefore important that older patients be screened extensively for any risk of vascular disease, infections, and occult malignancy before undergoing kidney transplantation.

In addition to screening the patient for suitability for transplantation, it is vital to prognosticate the risk on an individual basis so that a decision about live donation and staying on the waiting list for deceased donors can be made. In a large retrospective analysis on the scientific registry database, it was noted that patients with diabetes, blood group O and B, high

**Figure 5. Relative risk of infection and acute rejection in elderly transplant recipients**




**Reprinted with permission from Meier-Kriesche HU, et al. Increased immunosuppressive vulnerability in elderly renal transplant recipients. *Transplantation* 2000; 69:885–889.**

plasma renin activity (≥30 percent), and African American race and— patients on dialysis at listing—were more likely to die while on the waiting list and were therefore more likely to benefit from live donor kidney transplantation (7). In addition, the considerable variation in mortality that exists in dialysis patients on the waiting list depending upon the United Network Organ Sharing region, is also critical to decision making about live donation versus staying on the waiting list.

## How should we manage immunosuppression in the elderly?

Immunosuppressive therapy modification is particularly important in elderly patients, because aging has been associated with a higher risk of infectious complications and a lower risk of acute rejection episodes. In a retrospective analysis of 73,707 kidney transplant patients from 1988 to 1997, the incidence of death due to infection was six times higher and the incidence of graft loss was 1.5 times lower in elderly patients (Figure 5) (13).

In a retrospective cohort study performed at the University of Maryland, elderly patients who received standard immunosuppression (tacrolimus target level 10–12 ng/mL; mycophenolate mofetil 2 g/d) had a threefold higher risk of allograft loss and death compared with elderly patients who received less intense immunosuppresion (tacrolimus target level 8–10 ng/mL; mycophenolate mofetil 1 g/d). The acute rejection rates were similar in the 2 years of follow-up (14). Several factors could account for this difference. First, the pharmacokinetics and pharmacodynamics of the immunosuppressive agents change with age, notably a reduction in activity of the cytochrome IIIA family of isoenzymes that increases the bioavailability of calcineurin inhibitors. Second, older age leads to a gen-

eralized decrease in T cell proliferative responses, impaired IL-2 synthesis and expression on T cells, and increased IL-6 activity, all of which decrease immunogenicity and may be an explanation for fewer incidences of allograft rejection episodes in the elderly. Third, despite lower risk of acute rejection, chronic allograft fibrosis accounts for most cases of death-censored graft loss in the elderly. Although speculative, it is believed that older graft results in a senescence-related reduction in the reparative processes, worsens chronic changes such as fibrosis and vascular damage after transplantation, and eventually promotes allograft failure.

It is therefore imperative that immunosuppression be selected carefully in elderly patients, because both over- and underimmunosuppression are harmful. Consequently, IL-2 receptor antagonists are preferred over lymphocyte-depleting agents for the induction of immunosuppression in patients ≥60. Decreased target levels of tacrolimus and mycophenolate mofetil dose are recommended in the elderly to balance the risk of infection and acute rejection (14). Rapid steroid withdrawal is also recommended in the elderly, particularly in low-risk recipients. Because calcineurin inhibitors aggravate chronic changes, targeting lower levels of calcineurin inhibitors may increase allograft survival in elderly recipients.

---

Kidney transplantation can be considered the renal replacement therapy of choice in the older patient, provided that patient selection is appropriate. Because transplantation is associated with increased morbidity and mortality within the first 2 years, only patients with a life expectancy ≥2 years and good functional and cognitive status should be considered for kidney transplantation. Extensive pretransplantation screening for malignancies, infections, and vascular disease is mandatory, because death with a functioning allograft accounts for most cases of allograft loss in the elderly patient. It is also vital to tailor the immunosuppression in older patients to carefully balance the risk of infection and chronic allograft loss.

*Viresh Mohanlal, MBBS, and Matthew R. Weir, MD, are affiliated with the division of nephrology, department of medicine, at the University of Maryland Medical Center.*

**References**


1. USRDS: the United States Renal Data System. *Am J Kidney Dis* 2003; 42[6 Suppl 5]:1–230.
2. Harper AM, et al. The UNOS OPTN waiting list and donor registry. *Clin Transpl* 1998; 73–90.
3. Wolfe RA, et al. Comparison of mortality in all patients on dialysis, patients on dialysis awaiting transplantation, and recipients of a first cadaveric transplant. *N Engl J Med* 1999; 341:1725–1730.
4. Oniscu GC, Brown H, Forsythe JL. How great is the survival advantage of transplantation over dialysis in elderly patients? *Nephrol Dial Transplant* 2004; 19:945–951.
5. Rao PS, et al. Renal transplantation in elderly patients older than 70 years of age: results from the Scientific Registry of Transplant Recipients. *Transplantation* 2007; 83:1069–1074.
6. Huang E, et al. Intermediate-term outcomes associated with kidney transplantation in recipients 80 years and older: an analysis of the OPTN/UNOS database. *Transplantation* 2010; 90:974–979.
7. Schold J, et al. Half of kidney transplant candidates who are older than 60 years now placed on the waiting list will die before receiving a deceased-donor transplant. *Clin J Am Soc Nephrol* 2009; 4:1239–1245.
8. Port FK, et al. Donor characteristics associated with reduced graft survival: an approach to expanding the pool of kidney donors. *Transplantation* 2002; 74:1281–1286.
9. Ojo AO, et al. Survival in recipients of marginal cadaveric donor kidneys compared with other recipients and wait-listed transplant candidates. *J Am Soc Nephrol* 2001; 12:589–597.
10. Giessing M, et al. Outcomes of transplanting deceased-donor kidneys between elderly donors and recipients. *J Am Soc Nephrol* 2009; 20:37–40.
11. Remuzzi G, et al. Early experience with dual kidney transplantation in adults using expanded donor criteria. Double Kidney Transplant Group (DKG). *J Am Soc Nephrol* 1999; 10:2591–2598.
12. Doyle SE, et al. Predicting clinical outcome in the elderly renal transplant recipient. *Kidney Int* 2000; 57:2144–2150.
13. Danovitch GM, Gill J, Bunnapradist S. Immunosuppression of the elderly kidney transplant recipient. *Transplantation* 2007; 84:285–291.
14. Badowski M, et al. The impact of reduced immunosuppression on graft outcomes in elderly renal transplant recipients. *Clin Transplant* 2009; 23:930–937.

# Kidney End-of-Life Coalition: What Is It All About?

By Jean Holley

The end stage renal disease (ESRD) end-of-life coalition was developed by a diverse group of individuals committed to patient-centered end-of-life care for ESRD patients, their families, and their health care providers.

Between March 2000 and October 2001, a Robert Wood Johnson Workgroup focusing on end-of-life issues in the ESRD population addressed quality of life, quality of dying, and educational needs, culminating in a published report (1). The Workgroup developed three primary recommendations: 1) Centers for Medicare & Medicaid Services (CMS) should work with the ESRD Networks to coordinate and link dialysis and hospice care; 2) curricula on end-of-life care should be developed for nephrologists, nurses, social workers, dietitians, and technicians working in dialysis units and caring for patients and families with chronic kidney disease (CKD); and 3) networks should incorporate end-of-life care into educational outreach programs (1).

Network 5 embraced these recommendations and formed the Kidney End-of-Life (EOL) Coalition (www.kidneyeol.org). The coalition's goal is to promote effective interchange among patients, families, caregivers, payers, and providers in support of integrated patient-centered end-of-life care for chronic kidney disease patients (2). Initially the coalition was composed of workgroups (advance care planning, cardiopulmonary resuscitation, patient education, physician/clinician education, hospice, and website review) charged with delivering products to enhance end-of-life care for the target population.

Dedicated representatives from the major dialysis unit corporations, CMS, Network Forum, dialysis unit nurses, social workers, dietitians, technicians, nephrologists, midlevel providers, and administrators—working together under Network 5's oversight—composed the various workgroups. The coalition's website is the repository of these efforts and serves as a resource for anyone seeking information on end-of-life issues around CKD. Table 1 shows the categories of information and tools available on the coalition's website that can assist dialysis units and health care providers to deliver patient-centered end of life care.

ESRD is increasingly becoming a "geriatric" disease. The mean age of incident dialysis patients is slowly rising and the proportion of elderly dialysis patients is increasing (3). At the same time, however, there is increased recognition of the benefits and importance of palliative care, and growing emphasis on the consideration to withhold dialysis and medically manage some elderly patients with CKD (4, 5). The newly published revised Renal Physician Association (RPA) guideline, Shared Decision-Making in the Appropriate Initiation of and Withdrawal from Dialysis, includes new recommendations addressing the need to discuss prognosis with all patients beginning dialysis (6). In addition, the guideline recommends giving any patient older than 75 years with stage 5 CKD a specific estimate of prognosis so that the patient can make an informed decision about beginning dialysis (6).

Predictors of prognosis in elderly dialysis patients include functional status, comorbidity, nutritional status (based on serum albumin), and answering "no" to the so-called surprise question "Would I be surprised if this patient died within the next six months?" (6). Although elderly patients who begin dialysis generally live longer than those who forego dialysis (4, 5), most elderly patients on dialysis experience a significant worsening of functional status (7). Thus, all CKD patients, but especially the elderly and those with a poor prognosis, should be offered the option of palliative care and ongoing medical management without dialysis. The revised RPA guideline details factors involved in such decisions and provides toolkits to ensure that patients and families can make informed decisions about their options for renal replacement therapy, including time-limited trials of dialysis and active medical management without dialysis. The EOL Coalition website provides links to patient and physician resources related to these issues.

Palliative and end-of-life care is appropriate for all dialysis patients. The EOL Coalition incorporated components of ESRD palliative care through development of its workgroups and the delivered products that are available to assist nephrologists and dialysis units. ESRD palliative care includes advance care planning, pain and symptom management, bereavement care, and end-of-life care and hospice.

Advance care planning has evolved and is now recognized as a process that occurs primarily among patients and families as a means of addressing goals, achieving control over medical processes, and strengthening family relationships (8). Although writing some sort of advance directives remains a goal of advance care planning, the creation of advance directives is no longer the sole impetus driving the advance care planning process. Viable written advance directives include do not resuscitate (DNR) orders, health care surrogate or decision-maker designations, and, where available, physician orders for life-sustaining treatment (POLST).

The EOL Coalition website contains model policies for DNR orders, patient information sheets on cardiopulmonary resuscitation and resuscitation status, and links to other websites that provide information on specific advance directives (e.g., POLST forms) and states in which POLST is an available option. The CMS Conditions of Coverage now mandate that advance care planning be included in overall care plans for dialysis patients. The EOL Coalition is a valuable resource for dialysis units assessing and developing policies and procedures on advance directives and advance care planning.

## Hospice underused by dialysis patients

Nearly all nephrologists will care for patients who choose to stop dialysis. All patients withdrawing from dialysis are potential hospice candidates and should be offered hospice care. Yet hospice is a Medicare benefit that is underused by ESRD patients (9). Many other dialysis patients may also be candidates for hospice care if they have a non-ESRD diagnosis that is expected to lead to their death within the next six months.

The EOL Coalition and its members were instrumental in advocating for appropriate hospice benefits for ESRD patients and continue to assist in clarifying the options for hospice use among patients who wish to continue dialysis. One such option, and a tenet of hospice, is bereavement care, which is offered to families throughout the year following the death of the hospice

**Table 1. Information and tools on www.kidneyeol.org**

| | |
|---|---|
| **Guides** | Teaching patients about cardiopulmonary resuscitation<br>Planning dialysis unit memorial services<br>Funeral home information for dialysis units<br>Patient resuscitation statement |
| **Model policies for dialysis units** | Do not resuscitate (DNR)<br>Advance directives for DNR orders |
| **Links to organizations** | Medicare Benefit Policy Manual – ESRD<br>Center to Advance Palliative Care; National Hospice and Palliative Care Organizations<br>Advance Directives information, including Caring Connections<br>Renal Physicians Association and American Society of Nephrology position statements on quality care at the end of life<br>Renal Physicians Association "Shared Decision-Making in the Appropriate Initiation of and Withdrawal from Dialysis" |
| **Frequently asked questions** | |
| **Presentations** | PowerPoint slides on advance care planning, palliative care in ESRD |
| **Links to tools** | Dialysis Symptom Index<br>Edmonton Symptom Assessment System<br>Clinical algorithm and preferred medications to treat pain in dialysis patients<br>Assessing Decision-Making Capacity |
| **Links to patient information** | If You Choose Not to Start Dialysis (National Kidney Foundation)<br>When Stopping Dialysis Treatment is Your Choice (National Kidney Foundation)<br>Choosing to Stop Dialysis (Kidney Foundation of Canada)<br>Choosing Not to Start Dialysis (Kidney Foundation of Canada) |

patient. Many in the dialysis community have recognized the importance of bereavement care, not only for the families of patients who die, but also for the dialysis unit staff and allied providers. Memorial services are offered by many dialysis programs as part of bereavement care. The Coalition provides information to assist programs wishing to plan such services (Table 1).

Another component of ESRD palliative care is symptom assessment and management. The EOL Coalition produced and made available through its website several webinars addressing these issues (Table 2). In addition, the Coalition developed an evidence-based algorithm for pain management, which is also available on the website for use by clinicians. It is clear that symptom burden is high among dialysis patients and that their symptoms are undertreated (10). Incorporating palliative care into dialysis units should lead to improved recognition and treatment of patients through a focus on symptom assessment and management.

Providing dialysis care is not simply dialyzing individuals with kidney failure. Effective treatment must include assessment of the individual patient in accordance with his or her goals and values, quality of life, and, at some point for everyone, quality of dying. The increasingly aged dialysis population offers opportunities to consider traditional palliative care principles, such as hospice and end-of-life care, bereavement care, pain and symptom management, and advance care planning, for all of our patients through all stages of their chronic kidney disease. We are fortunate in dialysis care to work within an interdisciplinary team to provide comprehensive care for our patients. As with other important dialysis initiatives (e.g., Fistula First), nephrologists must assume leadership roles to ensure the success of this endeavor. Quality palliative and end-of-life care of CKD patients requires nephrologist leadership at the level of clinics and dialysis units. The RPA guideline (6) and the EOL Coalition are essential resources for nephrologists and other providers working with CKD and ESRD patients.

**References**


1. The Robert Wood Johnson Foundation. Promoting Excellence: End-Stage Renal Disease Workgroup Recommendations to the Field. http://www.kidneyeol.org.
2. Kidney End-of-Life Coalition. http://www.kidneyeol.org.
3. United States Renal Data System Annual Report 2010. http://www.usrds.org.
4. Carson RC, et al. Is maximum conservative management an equivalent treatment option to dialysis for elderly patients with significant comorbid disease? *Clin J Am Soc Nephrol* 2009; 4:1611–1619.
5. Murtagh FEM, et al. Dialysis or not? A comparative survival study of patients over 75 years with chronic kidney disease stage 5. *Neph Dial Transpl* 2007; 22:1955–1962.
6. Renal Physicians Association. *Shared Decision-Making in the Appropriate Initiation of and Withdrawal from Dialysis*, 2nd Ed., Rockville, MD, Renal Physicians Association, 2010.
7. Tamura MK, et al. Functional status of elderly adults before and after initiation of dialysis. *N Engl J Med* 2009; 361:1539–1547.
8. Singer PA, et al. Life-sustaining treatment preferences of hemodialysis patients: Implications for advance directives. *J Am Soc Nephrol* 1995; 6:1410–1417.
9. Murray AM, et al. Use of hospice in the United States dialysis population. *Clin J Am Soc Nephrol* 2006; 1:1248–1255.
10. Weisbord SD, et al. Prevalence, severity, and importance of physicial and emotional symptoms in chronic hemodialysis patients. *J Am Soc Nephrol* 2005; 16:2487–2494.


*Jean Holley, MD, is clinical professor of medicine at the University of Illinois at Urbana-Champaign.*

**Table 2. Educational material at www.kidneyeol.org**

| | |
|---|---|
| **Webinars** | Incorporating palliative care into the dialysis unit<br>Symptom assessment and management<br>Relevance of palliative care and hospice for dialysis patients<br>Pain assessment and management |
| **Pain management brochure** | |
| **Links** | Renal Palliative Care Bibliography<br>End-of-Life Decision-Making and the Nephrology Nurse—Educational Modules from American Nephrology Nurses Association<br>Robert Wood Johnson Promoting Excellence: ESRD Workgroup<br>Recommendations to the Field<br>Core Curriculum on Palliative Care for the Nephrologist |
| **PowerPoint presentations** | Advance Care Planning<br>Best Practices for End-of-Life Care for Dialysis Patients<br>Did This Patient Die in Hospice? New Questions in Caring for Patients with ESRD<br>End-of-Life Issues for ESRD Patients<br>ESRD: When is it Time for Hospice?<br>Hospice and ESRD: To Withdraw or Not to Withdraw<br>Pain Management in ESRD<br>Palliative Care for the ESRD Patient |

# Drug Dosing in the Elderly Patient with Chronic Kidney Disease

By Ali Olyaei

Chronic kidney disease (CKD) is a relatively common condition in the older American population. An estimated 26 million people in the United States are reported to have CKD. As the population of Americans 65 and older grows, so does the incidence of CKD. Evidence now indicates that kidney disease and aging carry a significant risk for cardiovascular complications and sudden death.

The progressive physiological changes with the aging process are inevitable: Aging-associated changes in carbohydrate metabolism and vascular atherosclerosis markedly increase the risk of developing diabetes and hypertension, and these high incidences of comorbid conditions may also lead to a higher incidence of cardiovascular events. Aging, directly or indirectly, has an effect on renal function and the handling of the most commonly used drugs in the geriatric population. The elderly with CKD are at a greater risk for adverse drug reactions and have a higher potential for drug–drug interactions (1, 2).

The pharmacokinetics and pharmacodynamics of most drugs are altered due to functional or anatomical changes of the renal system. These structural and functional changes are mostly multifactorial, resulting from the loss of kidney mass and exposure to precipitating factors leading to renal injury. These factors can include clinical nephrotoxins, electrolyte abnormalities, heart failure, and environmental insults.

In early adulthood, the average weight of a kidney is 250 g (±25 g); by age 75, kidney weight decreases to 200 g (±25 g). This loss of mass is most noticeable at the cortex level and much less in the medulla section. Glomeruli are also affected, with biopsies indicating a thickening basement membrane with hyalinization of renal arterioles. The incidence of biopsy-proven glomerulosclerosis increases from 1 to 2 percent in early adulthood, as opposed to roughly 30 percent by age 80+. Chronic vascular disease and inflammatory stages of CKD also contribute to tubular atrophy and interstitial fibrosis in the aging kidney. Other potential causes for loss of renal function could be due to aging-related vascular calcification, the release of endothelin-1 and nitric oxide synthase, free reactive oxygen species, and metabolic syndrome. Medication issues, including polypharmacy with the development of CKD, should also be considered for increased risk of morbidity and mortality (3).

Pharmacokinetics is the study of drug absorption, distribution, metabolism, and elimination. The drug dosing and adverse drug reactions observed in the aging CKD population is a complex combination of pharmacokinetic and pharmacodynamic variation from aging and CKD. Pathological or physiological adaptation of aging and CKD affects the pharmacokinetic behavior of most drugs. Therefore, health care providers must design a pharmacotherapeutic regimen for each patient to avoid unnecessary toxicity and

*Continued on page 20*

# Drug Dosing

*Continued from page 19*

overexposure to certain pharmacotherapeutic agents, while maintaining desirable pharmacotherapeutic outcomes. Table 1 summarizes the effects of aging on drug pharmacokinetics, and Table 2 shows the influence of CKD on the pharmacokinetics of most commonly used drugs. Unfortunately, most tables and protocols for drug dosing in renal impairment do not incorporate many elements of pharmacokinetic changes associated with CKD. These data are driven solely according to the renal elimination process (4).

**Table 1. Influence of aging on pharmacokinetics**

| Organ | Age-related changes |
|---|---|
| Kidney | Decreased GFR, renal blood flow, and tubular function |
| Liver | Decreased liver size and liver blood flow |
| Skin | Decreased hydration of stratum corneum, decreased skin surface lipids, and decreased skin microcirculation |
| Body | Decreased lean body mass, total body water, and body fat |

## Absorption

There appears to be no constant alteration in drug absorption in the elderly population or patients with CKD. However, oral iron therapy, calcium supplements, phosphate binders, gastroparesis, nausea, and vomiting related to uremia significantly alter the absorption of most drugs. For drugs requiring a rapid plasma concentration such as a loop diuretic or a narcotic analgesic, the edematous stage of the gastrointestinal tract may influence the pharmacodynamics of these agents. Uremia may decrease drug metabolism in the gastrointestinal area and increase bioavailabilities of some drugs, such as beta-blockers and narcotic analgesics. Aging may also affect transdermal drug absorption: Fentanyl patches may deliver doses at a higher concentration in older patients.

## Distribution

In contrast to drug absorption, the distribution of most drugs changes significantly in older patients with CKD. Both lean body mass and total body water decrease with age. However, CKD may increase the volume of distribution for hydrophilic agents, whereas the volume of distribution maintains or changes for lipophilic agents. These alternations may lead to higher or lower plasma concentrations. For example, gentamicin has a volume of distribution of 0.25 L/kg, which requires closer monitoring in the elderly with impaired renal function than younger patients with the same infection. Drugs are pharmacologically active only in the unbound stage, and are mostly bound to albumin or α-1-acid glycoprotein. In advanced age, albumin levels have a tendency to decrease whereas α-1-acid glycoprotein may increase. For drugs that are highly protein bound, CKD may alter the free unbound concentration. The protein binding of phenytoin is reduced in CKD or in patients with significant proteinuria. In the elderly with CKD, "therapeutic" plasma concentrations could be associated with drug toxicity due to increased free fraction or unbound drug concentration. Therefore, plasma concentration should be adjusted according to albumin level and stage of CKD (4).

## Metabolism

Most drugs are excreted unchanged through the kidney, or metabolized through phase I or II reactions. Phase I reactions involve drug oxidation, reduction, and hydrolysis. Cytochrome P-450 also plays an important role in phase I reactions. Phase II metabolism involves glucuronidation, sulfation, acetylation, and methylation. Both aging and CKD reduce the hepatic clearance of many drugs. Phase I reactions are substantially decreased with aging, which has a smaller effect on phase II reactions. Liver mass is approximately 20 to 40 percent lower in elderly patients, with significantly reduced liver blood flow. Uremia may also influence the expression of the cytochrome P-450 isoenzyme system so that patients with CKD cannot metabolize drugs completely. Elderly patients with CKD may achieve a higher plasma concentration or even toxic concentrations of pharmacologic agents when they are prescribed at approved dosages.

Many drugs that metabolize, inhibit, or induce the cytochrome P-450 system and adverse drug reactions due to potential enzyme inhibition are common in older patients with CKD. Despite all of these fluctuations in pharmacokinetic properties due to drug metabolism, clinically, there is no quantitative approach to adjusting drug dosage according to liver function in older patients or patients with CKD. As a result, drug-induced liver injury is more common in the elderly (5).

**Table 2. Influence of chronic kidney disease on pharmacokinetics**

| Pharmacokinetics parameter | Kidney disease effects | Incorporated into drug dosage |
|---|---|---|
| Drug absorption | + | No |
| Volume of distribution | ++ | No |
| Intestinal and first pass metabolism | + | No |
| Distribution | ++ | No |
| Elimination | | |
| Renal | +++ | Yes |
| Nonrenal | ++ | No |

## Elimination

Reduced renal function may prolong drug half-life and increase the risk of toxicity. To avoid drug toxicity, an accurate estimate of renal function is essential. As mentioned, kidney function generally declines with age. Renal blood flow, tubular function, and filtration are significantly reduced by 70 to 80 years of age. Risk factors for developing drug-induced kidney disease include female gender, age, dehydration, CKD, diabetes, cardiovascular disease, and end stage liver disease. Despite many hopes, there is no reliable clinical predictor of nephrotoxicity in elderly patients. In general, after the age of 30, creatinine clearance (CrCl) declines by 1 mL/min/year with a much higher rate for hypertensive and diabetic patients. The glomerular filtration rate (GFR) is a good overall index of kidney function in both healthy patients and those with CKD.

Clinically, the measurement of GFR is difficult and cumbersome, and has traditionally been estimated using age, weight, serum creatinine, race, and gender. Several methods of estimating GFR have been recommended. CrCl is the most common method, using the Cockcroft and Gault (CG) equation. The CG equation was developed in 1976 from a study of 249 Caucasian males, with and without CKD. Four main factors affect this equation: age, weight, creatinine, and gender. The CrCl using this method tends to overestimate GFR because of the tubular secretion of creatinine (6–8).

$$\text{Estimated creatinine clearance (mL/min)} = \frac{1.2 \times (140 - \text{age [year]}) \times \text{weight (kg)}}{\text{Serum creatinine (μmol/L)}} \quad (\times\ 0.85 \text{ for women})$$

In 1999, the Modification of Diet in Renal Disease (MDRD) equation was introduced to estimate renal function in patients with CKD. This study was conducted in both men and women, all with CKD. MDRD is less accurate in patients with GFR >60 mL/min; however, it is a more accurate measurement of GFR than CG in patients with GFR <60 mL/min. There are two methods of estimation: four-point (age, gender, race, creatinine) and six-point (age, gender, creatinine, BUN, albumin, race). The four-point equation is as follows:

GFR = 186.3 × SerumCr – 1.154 × age – 0.203 × 1.212 (if patient is black) × 0.742 (if female)

The MDRD equation for estimating GFR using the six-point method can be calculated as:

$$\text{GFR (mL/min/1.37m}^2) = 170 \times [P_{CR}]^{-0.999} \times [\text{Age}]^{-0.176} \times [\text{SUN}]^{-0.170} \times [\text{Alb}]^{+0.318} \times 0.762 \text{ **if patient is female**} \times 1.180 \text{ **if patient is black**}$$

where $P_{CR}$ = serum creatinine concentration (mg/dL), Age = age of the patient (years), SUN = serum urea nitrogen (mg/dL), and Alb = serum albumin concentration (g/dL).

In 2009, the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation was released. The CKD-EPI equation is a modified MDRD equation with a more accurate estimate of renal function in patients with CKD for both impaired renal function and patients with GFR >60 mL/min. The CKD-EPI equation takes into account age, creatinine, gender, and race and is calculated as follows:

GFR = 141 × min(Scr/κ,1)α × max(Scr/κ, 1) – 1.209 × 0.993Age × 1.018 [if female] × 1.159 [if black]

where Scr = serum creatinine (mg/dL), κ = 0.7 for females and 0.9 for males, α = –0.329 for females and –0.411 for males, min = minimum of Scr/κ or 1, and max = maximum of Scr/κ or 1.

Other methods to measure GFR include a 24-hour urine collection, which is inconvenient for most patients, or the measurement of cystatin C (an endogenous marker), which has not been validated for drug dosing.

These calculations can be downloaded from a number of mobile medical applications from http://www.qxmd.com/calculate-online/nephrology or http://nephron.com for iPhone, iPad, and BlackBerry. It has been speculated that the MDRD method of GFR estimation may improve precision, reduce variation in estimating kidney function, and lead to more consistent drug dosing. However, for most drugs, MDRD equations have not been validated. All of these methods are often found to under- or overestimate renal function. For drug dosing in patients with CKD or the elderly, and in particular for patients with mild renal insufficiency, the MDRD and CKI-EPI equations provide less reliable estimations of renal function than the CG equation, and all three methods lack precision.

## Prescribing in the elderly with CKD

Pharmacotherapy drug response in the elderly is associated with significant intra- and interindividual variability. Medication management in the elderly with chronic kidney disease is a challenging task. Pharmacokinetic and

pharmacodynamic variability associated with aging and CKD should be incorporated into the treatment plan for optimal therapy. A clinical treatment plan should include the type and severity of kidney disease, comorbid conditions, level of renal function, drug interactions, and cost. There are no simple rules for drug dosing in CKD that can be applied to the elderly population. If possible, for most medications, the advice is: "Start slow and go slower." For infection complications, however, health care providers need to be more aggressive about providing optimal care while reducing adverse drug reactions. If possible, providers should follow these steps:

1. Take a careful medical and drug history
2. Consider adverse drug reactions or potential contraindications
3. Give a loading dose to reach therapeutic drug concentration rapidly
4. Adjust a maintenance dose according to renal function (http://kdp.louisville.edu/renalbook/)
5. Adjust schedule according to renal function (http://kdp.louisville.edu/renalbook/)
6. Consider therapeutic drug monitoring if possible (Table 3)
7. Detect drug interactions and adverse drug interactions

## Conclusion

Pharmacotherapy in the elderly with CKD remains a challenging task. Rational drug therapy for elderly patients with CKD requires an adequate knowledge of disease status, comorbid conditions, and the pharmacokinetic and pharmacodynamic properties of the selected drug. Understanding the time course of drug effects (absorption, distribution, metabolism, and elimination) is vital for avoiding drug toxicity while optimizing the clinical outcome.

**References**


1. Rifkin DE, Winkelmayer WC. Medication issues in older individuals with CKD. *Adv Chronic Kidney Dis* 2010; 17:320–328.
2. Stegemann S, et al. Geriatric drug therapy: neglecting the inevitable majority. *Ageing Res Rev* 2010; 9:384–398.
3. Williams BR, Kim J. Medication use and prescribing considerations for elderly patients. *Dent Clin North Am* 2005; 49:411–427.
4. Olyaei AJ, Bennett WM. Drug dosing in the elderly patients with chronic kidney disease. *Clin Geriatr Med* 2009; 25:459–527.
5. Seripa D, et al. Pharmacogenetics of cytochrome P450 (CYP) in the elderly. *Ageing Res Rev* 2010; 9:457–474.
6. Levey AS, Stevens LA. Estimating GFR using the CKD Epidemiology Collaboration (CKD-EPI) creatinine equation: more accurate GFR estimates, lower CKD prevalence estimates, and better risk predictions. *Am J Kidney Dis* 2010; 55:622–627.
7. Stevens LA, et al. Comparative performance of the CKD Epidemiology Collaboration (CKD-EPI) and the Modification of Diet in Renal Disease (MDRD) Study equations for estimating GFR levels above 60 mL/min/1.73 m2. *Am J Kidney Dis* 2010; 56:486–495.
8. Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. *Nephron* 1976; 16:31–41.


*Aly Olyaei, PharmD, is professor of medicine and pharmacotherapy in the division of nephrology and hypertension at Oregon State University.*

**Table 3. Therapeutic drug monitoring in chronic kidney disease**

| Drug | Therapeutic range | When to draw sample | How often to draw levels |
|---|---|---|---|
| Aminoglycosides (gentamicin, tobramycin, amikacin)<br>Conventional dosing<br>24-hour dosing | Gentamicin and tobramycin:<br>Trough: 0.5–2 mg/L<br>Peak: 5–8 mg/L<br>Amikacin:<br>Peak: 20–30 mg/L<br>Trough: <10 mg/L<br>0.5–3 mg/L | Trough: immediately prior to dose<br>Peak: 30 min after a 30- to 45-min infusion<br>Obtain random drug level 12 hours after dose | Check peak and trough with third dose<br>For therapy <72 hours, levels not necessary<br>Repeat drug levels weekly or if renal function changes<br>After initial dose.<br>Repeat drug level in 1 week or if renal function changes |
| Carbamazepine | 4–12 µg/mL | Trough: immediately prior to dosing | Check 2–4 days after first dose or change in dose |
| Cyclosporin | 150–400 ng/mL | Trough: immediately prior to dosing | Daily for first week, then weekly |
| Digoxin | 0.8–2.0 ng/mL | 12 hours after maintenance dose | 5–7 days after first dose for patients with normal renal and hepatic function; 15–20 days in anephric patients |
| Lidocaine | 1–5 µg/mL | 8 hours after iv infusion started or changed | |
| Lithium | Acute: 0.8–1.2 mmol/L<br>Chronic: 0.6–0.8 mmol/L | Trough: before a.m. dose at least 12 hours since last dose | |
| Phenobarbital | 15–40 µg/mL | Trough: immediately prior to dosing | Check 2 weeks after first dose or change in dose.<br>Follow-up level in 1–2 months |
| Phenytoin, free phenytoin | 10–20 µg/mL<br>1–2 µg/mL | Trough: immediately prior to dosing | 5–7 days after first dose or after change in dose |
| Procainamide, N-acetyl procainamide (a procainamide metabolite) | 4–10 µg/mL<br>Trough: 4 µg/mL<br>Peak: 8 µg/mL<br>10–30 µg/mL | Trough: immediately prior to next dose or 12–18 hours after starting or changing an infusion<br>Draw with procainamide sample | |
| Quinidine | 1–5 µg/mL | Trough: immediately prior to next dose | |
| Sirolimus | 10–20 ng/dL | Trough: immediately prior to next dose | Daily for first week, then weekly |
| Tacrolimus (FK-506) | 10–15 ng/mL | Trough: immediately prior to next dose | Daily for first week, then weekly |
| Theophylline po or aminophylline iv | 15–20 µg/mL | Trough: immediately prior to next dose | |
| Valproic acid (divalproex sodium) | 40–100 µg/mL | Trough: immediately prior to next dose | Check 2–4 days after first dose or change in dose |
| Vancomycin | Trough: 5–15 mg/L<br>Peak: 25–40 mg/L | Trough: immediately prior to dose | With third dose (when initially starting therapy, or after each dosage adjustment)<br>For therapy <72 hours, levels not necessary<br>Repeat drug levels if renal function changes |

# Practice Pointers

# Geriatric Nephrology

*In this month's issue,* ASN Kidney News *editorial board member Edgar Lerma interviewed Jean Holley, clinical professor of medicine at the University of Illinois, Urbana-Champaign, about kidney care for the elderly patient.*

**Please describe the epidemiology of chronic kidney disease (CKD) in the elderly.**

The elderly CKD population is growing rapidly, and there is a corresponding increase in the number of elderly patients on dialysis. Most studies of the elderly with CKD and end stage renal disease (ESRD) show a survival benefit for the elderly who begin dialysis, except for those with ischemic heart disease in whom dialysis does not appear to extend survival. Unfortunately, although some elderly do well on dialysis, most elderly dialysis patients experience a progressive decline in functional status with repeated hospitalizations, increasing symptom burden, and caregiver stress. A few small studies examining survival in elderly who choose a conservative or palliative course over renal replacement therapy show a generally shorter survival for those refusing dialysis but fewer days of hospitalization.

**When did we start doing conventional dialysis in nursing homes?**

I'm not sure when the first dialysis treatment was performed in a nursing home, but there are many dialysis programs that have been operating in nursing homes for over 30 years. Increasingly, there are hemodialysis centers located in extended care facilities offering hemodialysis to residents with ESRD, but most of the published literature on dialysis in nursing homes describes peritoneal dialysis (PD) programs. Likely because of the comparative technical ease of PD compared with hemodialysis (for both the patients and the providers), PD in nursing homes has existed since the late 1980s.

**Is any one form of dialysis better than the other in elderly individuals?**

In general, no. I don't think one form of dialysis is better than another for elderly individuals who require dialysis. Some may disagree with me and argue that PD should be the preferred modality owing to less hemodynamic stress with PD. Others may argue that learning PD is difficult for the elderly and that hemodialysis is therefore the preferred modality. As with younger patients, I think, for specific individuals, one form of dialysis may certainly be preferable to another. Selecting the dialysis modality for an individual is based on shared decision making among the patient and family, nephrologist, and dialysis educators, be they nurses, social workers, or peer counselors.

For certain elderly with CKD, transportation to and from hemodialysis units may be problematic and for them, home PD may be the better option. For other elderly individuals, getting out of the home and experiencing the social interactions inherent in in-center hemodialysis may be a reason to select hemodialysis. Certainly medical conditions and comorbid illnesses will influence modality choice in some individuals, e.g., permanent arteriovenous access options for hemodialysis, hemodynamic status and cardiovascular disease, cognitive function, and ability to learn and perform PD, but, as with younger CKD patients, lifestyle preferences will usually dictate modality choice. Most of us have had elderly patients who do well on either modality.

**What are the pros and cons of doing dialysis in the nursing home? Reimbursement issues? Personnel issues?**

Nursing home patients who undergo dialysis where they live avoid the stresses and discomfort of transport to a dialysis center. If on assisted PD, they are able to have PD without doing the procedure themselves. Although rates of PD-associated infections vary among programs, patients on PD in nursing homes seem to have peritonitis rates comparable to home-living PD patients. Training nursing home staff to perform dialysis can be a major barrier if there is rapid staff turnover. The nursing home must also have ample storage space for PD supplies.

There are fewer reports of hemodialysis performed in nursing homes but patient survival appears to be comparable to similar patients (elderly, functionally dependent, commonly diabetic) dialyzing in outpatient units. Because of the patient population, indwelling catheters may be more commonly used as hemoaccess. Reimbursement issues for nursing home–based dialysis have not been discussed in the literature. Nursing home–based hemodialysis would presumably be administered and reimbursed, as would any hemodialysis unit. Nursing home–based PD usually requires a formal agreement between the nursing home and the dialysis program providing the staff training. This agreement will also include methods for providing PD supplies, patient laboratory testing, and nephrologist visits. In most cases, the dialysis program will be responsible for billing for the dialysis.

**Knowing that renal replacement therapy is a life and death decision, what other nondialytic options can be offered to an elderly individual who refuses this modality?**

CKD patients who refuse dialysis should receive ongoing palliative or conservative care. For some of these patients, hospice care may be an option (if expected survival is <6 months). Management of CKD in patients choosing not to undergo dialysis may include continuing therapies designed to slow progression of CKD, treatment of anemia, and advance care planning. Care is directed toward symptom management, maximizing quality of life, and appropriate preventive strategies, such as reducing frailty and falls. If, in the opinion of the patient's primary care physician and nephrologist, the patient is expected to live less than six months, the patient may be considered for hospice care, which would entail an assessment by the local hospice program.

**What is renal palliative care? What does it entail?**

Palliative care is generally described as patient and family-centered care that optimizes quality of life by preventing and treating suffering, including physical, emotional, and spiritual suffering. Renal palliative care focuses on identifying and treating causes of suffering. Palliative care can include advance care planning, pain and symptom management, and bereavement care. Renal palliative care encompasses the ongoing medical care given to CKD patients who choose not to begin dialysis as well as the routine palliative care of dialysis patients.

Quality improvement projects conducted in dialysis programs may also be directed at palliative care (e.g., review of patient deaths to determine if hospice referral was appropriate or review of resuscitation policies and recording of do not attempt resuscitation status of patients). Many dialysis units hold yearly or semiannual bereavement programs or send sympathy cards to families of patients who die—these are both examples of bereavement care as a component of renal palliative care. Because we cannot cure CKD, palliative care is the basis of our overall care of CKD and ESRD patients. Formally recognizing the components of palliative care will hopefully focus our efforts in this direction for our patients.

**What are the common reasons for discontinuing dialysis in an elderly individual?**

I think there are two distinct situations in which dialysis is discontinued. One is in the acute setting, after a medical complication or illness such as cerebrovascular accident, an episode of sepsis, or a cardiovascular event. Commonly in such circumstances, prognosis is extremely poor and the patient—or more commonly the health care surrogate or family (because the patient is not capable of decision-making)—chooses to stop dialysis. Death in such cases often occurs within hours or one to two days and usually while the patient is in the hospital. The other situation typically involves a patient-driven decision to stop dialysis, often due to an increasing burden of disease and progressively diminishing quality of life. In the absence of significant residual kidney function, death usually occurs within eight to 10 days of stopping dialysis in such patients. Hospice care should be offered to these patients.

The literature suggests that patients withdraw from dialysis because of unacceptable quality of life and the burdens of dialysis. Such patients are usually white, older, often diabetic, and often of higher socioeconomic and educational status. In such cases, it is hoped that appropriate palliative care interventions were performed to treat symptoms and physical, emotional, and spiritual suffering before the decision to stop dialysis was made. Sometimes, despite our best efforts and palliative care, the quality of life cannot be improved sufficiently to outweigh the burdens of ongoing suffering.

**What are the intricacies regarding hospice and Medicare benefits?**

Hospice and chronic dialysis are both Medicare benefits, so most hospice programs will not accept patients for whom the hospice diagnosis is ESRD if the patient wishes to continue dialysis; in that case, the hospice program would be responsible for the payment of the dialysis treatments. An ESRD patient with a diagnosis other than ESRD can be admitted to hospice and continue dialysis (e.g., a patient with metastatic lung cancer who wishes to enroll in hospice but wants to continue routine hemodialysis treatments). Individual hospice programs may differ in their acceptance of this pa-

tient but, in this scenario, the Medicare hospice benefit would occur under the diagnosis of lung cancer. Dialysis could continue under the ESRD diagnosis—the hospice program would not be responsible for the dialysis costs. Thus, the diagnosis under which a patient is admitted to hospice will determine the hospice program's responsibility for dialysis costs. The acceptance of this patient into the hospice program is based on financial and administrative factors.

Some have argued that hospice should be available to patients who wish to continue dialysis, even in the absence of a diagnosis other than ESRD, and some hospice programs may consider such a patient—but the cost of dialysis to the hospice program is usually prohibitive. Most social workers in dialysis units are aware of these issues and can be valuable resources to patients, families, and providers.

### What is the "Kidney End of Life Coalition"?

I'll refer you to my article in this issue for a complete answer to this question (p. 18). The brief answer is that the Coalition is a resource center (www.kidneyeol.org) for patients, families, and dialysis units and all who work in them. The focus of the Coalition is end-of-life and palliative care for CKD and ESRD patients.

### Are there resources you would recommend for dealing with these difficult ethical aspects of nephrology practice—for physicians, patients, dialysis staff, and providers?

The two most useful resources are the Kidney End-of-Life Coalition website, www.kidneyeol.org, and the clinical practice guideline published by the Renal Physicians Association, *Shared Decision-Making in the Appropriate Initiation of and Withdrawal from Dialysis* (2nd edition, Oct. 2010, available from the Renal Physicians Association at www.renalmd.org for $50.00 for an RPA member, $149.00 for a nonmember). The guideline provides 19 recommendations for withholding and withdrawing dialysis in adult and pediatric patients with acute kidney injury, CKD, and ESRD. It is a consensus expert opinion based on ethical principles, case and statutory law, and a systematic review of the published literature by dedicated volunteers. Practical toolkits for assessing cognitive function, capacity, prognosis, symptoms, and dealing with the difficult patient are included in the guideline. Guideline recommendations address advance care planning, informing patients and families, making decisions not to initiate or to discontinue dialysis, and providing palliative care. It is an invaluable resource for patient care in this area of nephrology.

### Please give us some practice pointers for dealing with elderly patients on dialysis.

1. Provide patients with information on prognosis when discussing renal replacement therapy. Increasingly, we are realizing that it is our job to provide some prognostic information to all of our patients, but especially our elderly patients with CKD. In order to make an informed decision about starting, withholding, or stopping dialysis, patients need to be given information on prognosis and likely clinical outcomes, just as they are given information on modality options. It is the nephrologist's job to provide that information.
2. Time-limited trials of dialysis should be used, but it is incumbent upon the nephrologist to readdress dialysis with the patient after the four- to six-week trial to determine the patient's desire to continue on dialysis. Don't assume that if the patient says nothing, he or she wishes to continue dialysis.
3. Initiate discussions about end-of-life care and advance care planning with patients. Most patients assume physicians will bring up these issues. Communicating with patients and families is an integral aspect of shared decision-making and the skills required improve with practice. If you're not now and will likely never be comfortable with such discussions, identify someone in the dialysis unit who is and employ their skills.
4. Patients who stop dialysis should be referred for hospice care if the patient and family desire it.
5. Be a leader in palliative care initiatives in the dialysis unit. Our patients and staff deserve our attention to these issues.

### Suggested Reading


1. Reddy NC, et al. Staff-assisted nursing home haemodialysis: patient characteristics and outcomes. *Nephrol Dial Transpl* 2007; 22:1399–1406.
2. Taskapan H, et al. Peritoneal dialysis in the nursing home. *Int Urol Nephrol* 2010; 42:545–551.
3. Anderson TE. Ten years' experience with CAPD in a nursing home setting. *Perit Dial Int* 1997; 17:255–261.
4. Tong EM, Nissenson AR. Dialysis in nursing homes. *Semin Dial* 2000; 15:103–106.

# Policy Update

## Quality Improvement Program Rule Addresses Key ASN Recommendations

By Rachel Shaffer

Finalizing performance standards and scoring methodology for the Quality Improvement Program (QIP), the Centers for Medicare and Medicaid Services (CMS) issued a QIP Final Rule on December 29, 2010. CMS will implement the QIP—the first-ever mandatory pay-for-performance program within CMS—on January 1, 2012. The second major change to the Medicare ESRD program, CMS will institute the QIP exactly one year after implementing the new bundled Prospective Payment System (PPS) last month.

CMS sought public comment on a QIP Proposed Rule during the summer of 2010. ASN formed a Task Force that analyzed and provided feedback on this initial proposal composed of experts and ASN Advisory Group members. In the recently released QIP Final Rule, CMS addressed several of ASN's key concerns and suggestions. Chief among these is the establishment of a monitoring system—a direct response to ASN's advocacy—as well as an agreement to work with the ESRD community through a formal rule-making process should CMS pursue any substantive changes to the QIP, including adoption of new measures, weights, or performance standards.

### Quality measures

The three quality measures against which facilities will be measured during the first year of the QIP were finalized in the ESRD PPS Final Rule, which CMS also released in July, 2010 (Table 1). The final QIP rule reiterated this decision, but also noted that CMS anticipates replacing the average urea reduction ratio (URR) measure with a measure of Kt/V in the future. Furthermore, CMS states that it is in the process of developing "to the extent feasible" other measures that could be applied to all modalities including patient satisfaction, iron management, bone and mineral metabolism, vascular access, and fluid weight management.

### Performance standards

CMS finalized its proposal to compare facilities' data during the performance period to the lesser (more lenient) of the two following standards:

1. the facilities' own performance on each measure during 2007, or
2. the national performance rates of all dialysis providers, calculated from 2008 data (Table 2)

CMS also finalized its proposal to establish the "performance period" as the entire calendar year of 2010—meaning that the payment reductions providers see beginning January 1, 2012, will be based on their performance in 2010. CMS indicated it will use the year 2011 to analyze 2010 data, determine which facilities met the performance standards, and allow providers time to review their performance scores before applying payment reductions during the "consequence period," January 2012. (Figure 1).

### Performance scores and payment reductions

CMS made no changes to the scoring methodology it laid out in the QIP proposed rule. It will assign 10 points to each of the three quality measures, with facilities that meet or exceed performance standards earning a total of 30 points. For every percentage point a facility falls below one of the three standards, CMS will subtract up two points (in increments of 0.5 points) from the 30 possible total.

Additionally, CMS will weight the "hemoglobin <10 g/dL" measure as 50 percent of the total performance score. It notes that this approach establishes a disincentive for providers to undertreat patients for anemia. This is important in light of the new ESRD bundled payment system, under which administration of the drugs that treat anemia—erythropoeisis stimulating agents (ESAs)—is now a cost center rather than a source of profit for dialysis facilities. The remaining 50 percent of the total performance score will be divided equally between the two other measures. CMS noted that it will reevaluate this methodology as it adopts new quality measures in the future.

### Public reporting

Under the QIP, every dialysis facility will be required to publicly post a certificate displaying data related to all three quality measures, as well as comparative data showing how well the data compare to national performance rates. This information will also be publicly available via CMS' Dialysis Facility Compare website.

### New monitoring plan

Along with other commentators, ASN emphasized that "careful monitoring in as close to real-time as possible will be crucial to the success of the QIP by minimizing adverse unintended consequences, including compromises in access to care" in its comments to CMS regarding the proposed rule. Responding directly to this concern, CMS stated in the final rule that it will "launch an ESRD services monitoring program to identify changes in beneficiary access to, and the quality of care, following the implementation of the ESRD PPS in 2011 and the QIP in 2012."

CMS announced it will also undertake a long-term evaluation, examining relationships between ESRD and QIP policies and patient outcomes for vulnerable subpopulations. While the final rule does not provide extensive detail on monitoring or evaluation activities, it notes that CMS will utilize CROWNWeb, claims data, patient activity reports, and other quantitative and qualitative sources.

The ASN Public Policy Board and policy staff will continue to work closely with CMS to address any remaining concerns regarding the QIP leading up to its implementation, as well as to offer guidance as CMS refines plans for monitoring and evaluation activities. To read the complete QIP final rule and access other ESRD bundling-related resources, please visit www.asn-online.org/policy_and_public_affairs..

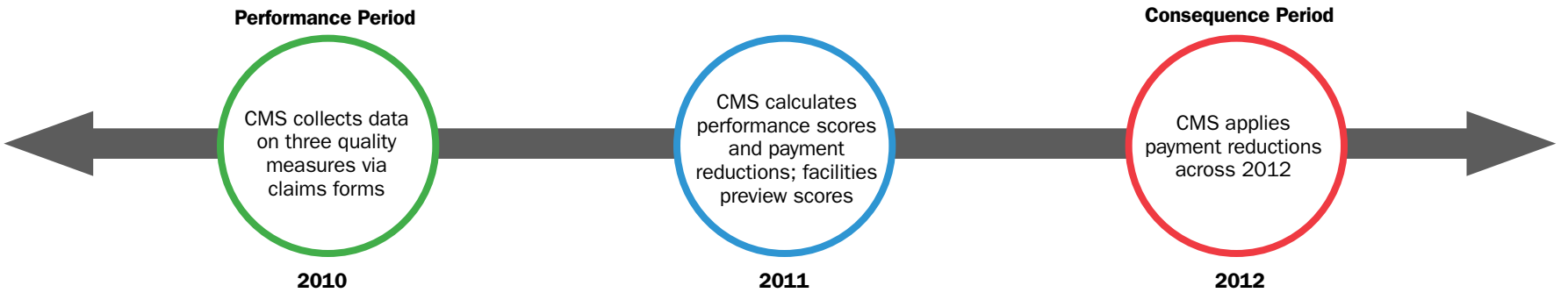
**Table 1. QIP quality measures for 2012**

- Hemodialysis adequacy: percentage of Medicare patients with an average urea reduction ratio (URR) of 65 percent or more
- Anemia management: controlled anemia, as shown in two measures:
  - The Medicare percentage of patients at a facility whose hemoglobin levels were <10 g/dL
  - The percentage of Medicare patients at a facility whose hemoglobin levels were >12 g/dL.

**Table 2. 2008 National Performance Rates (percentage of Medicare patients who achieved the following average values in 2008)**

- Hemodialysis adequacy (URR ≥ 65%): 96 percent
- Hemoglobin <10 g/dL: 2 percent
- Hemoglobin >12 g/dL: 26 percent

**Figure 1. Timeline of performance and consequence periods**



# Journal View

## Population Screening for CKD Isn't Cost-Effective

One-time screening for chronic kidney disease (CKD) in the general population is not a cost-effective intervention, reports a study in the *British Medical Journal*.

Using laboratory data from the publicly funded Canadian health system, the researchers compared a strategy of population screening for CKD—based on one-time measurement of estimated glomerular filtration rate—versus no screening. The model accounted for incidentally detected cases of CKD and was stratified for age, diabetes, and proteinuria. The main outcome measures were lifetime costs, occurrence of ESRD, quality-adjusted life-years (QALYs) gained, and incremental cost per QALY gained.

Compared to no CKD screening, one-time population screening carried an incremental cost of $C493 (US $382). The overall net gain of screening was 0.0044 QALYs per patient, at a cost of $C104,900 per QALY. This was significantly higher than the accepted cost for other interventions funded by public health care systems.

On subgroup analysis, CKD screening was cost-effective in patients with diabetes: cost per QALY gained $C22,600, compared to $C572,000 in those without diabetes. Screening was not cost-effective for patients with hypertension but without diabetes, or in nondiabetic older adults. Based on evidence showing the benefits of angiotensin blockade for diabetic patients with CKD, screening of patients with diabetes would lead to significantly improved clinical outcomes.

Screening for CKD is already recommended for certain high-risk groups, including patients with diabetes or hypertension and those aged 60 years or older. Some guidelines have recommended population-based CKD screening, which has already been implemented in a few countries.

However, the new study questions the cost-effectiveness of one-time, laboratory-based CKD screening. Screening does not appear cost-effective in the overall population, or even in subgroups defined by hypertension or older age. Targeted screening for CKD in patients with diabetes is cost-effective, with effective treatments leading to better clinical outcomes. [Manns B, et al. Population based screening for chronic kidney disease: cost-effectiveness study. *BMJ* 2010; 341: c5869].

# NIDDK: Planning for the Future

## *This is the last in a three-part series looking at the NIDDK and its impact on kidney research*

The National Institutes of Diabetes and Digestive and Kidney Diseases (NIDDK) celebrated its 60th anniversary in 2010. Taking the opportunity offered by this milestone, NIDDK has begun a thoughtful look at its strategic pathway for kidney disease research. The result is the "Kidney Research National Dialogue (KRND)," a project undertaken to chart the most robust strategic plan to advance kidney disease research as the institute looks ahead to a new decade.

At its core, the KRND seeks to identify the key research questions that—if answered—provide the most benefit to scientists researching the causes, progression, and treatment of kidney disease. The initiative encompasses three phases.

The first phase—running through March 2011—asks participants to suggest questions or objectives of critical importance for kidney disease research moving forward. The dialogue also allows participants to discuss, assess, and rank suggestions from other participants. Following completion of the first phase, NIDDK will combine and summarize the suggestions that received the highest rankings.

The second phase of the initiative, to begin in March 2011, will ask participants to decide on strategies to bring the research suggestions from phase I to fruition. NIDDK anticipates that some research strategies may require groundwork research before the larger question can be studied; however, all forms of translational, clinical, and basic research will be considered when designing strategies in phase II.

The final phase of the KRND will begin in May 2011. NIDDK will collect the results of the first two KRND phases and combine them into one comprehensive Blueprint for Kidney Research publication that will be publically available.

The KRND is open to any interested physicians, patients, or researchers and began in November 2010.

"NIDDK, in deciding to take a fresh look at the strategic plan for kidney disease research, has provided a significant opportunity for kidney disease research participants and advocates to greatly impact the future direction of the field, hopefully assisting NIDDK in committing valuable dollars to areas which provide the highest promise and greatest impact for patients with kidney disease," said John Sedor, MD, chairman of the ASN Research Task Force and NIDDK Councilor.

While the Kidney Research National Dialogue promises to guide kidney research at NIDDK in the coming decade, the immediate outlook for research funding remains somewhat unsettled as a final budget for fiscal year (FY) 2011 has not yet been passed by Congress. Currently, NIDDK is operating under a continuing resolution passed by Congress in December 2010. The continuing resolution essentially keeps funding stable at FY2010 levels through March 4, 2011.

Moving forward, it is unclear what cuts, if any, the FY2011 budget will include. While some budget cuts are anticipated, they are far from certain. As described by ASN Public Policy Board Chairman Thomas Hostetter, MD, the magnitude of kidney disease research funding is far-reaching.

"The importance of strong, continued federal research funding cannot be understated, in addition to the benefits derived by patients, research funding also spurs job creation across the country." ASN continues to advocate for robust, sustained research funding for NIH as well as other federal agencies. To learn more about ASN Advocacy or the Kidney Disease National Dialogue, visit ASN Policy. (http://www.asn-online.org/policy_and_public_affairs/medical-research.aspx)

## Index to Advertisers

# Kidney Expert Addresses CKD Research Advances, CKD Care, and Health Care Changes

***ASN Kidney News spoke with Michael Chonchol, MD, at Renal Week 2010 about chronic kidney disease (CKD), research advances in CKD, and the coming changes in kidney health care. Chonchol is associate professor of medicine and a nephrologist with the division of renal diseases and hypertension at the University of Colorado School of Medicine in Denver.***

Twenty-six million Americans have kidney disease, defined by protein in the urine and a glomerular filtration rate (GFR) of 60 or less for three months. The biggest risk factors for developing CKD are diabetes and hypertension. Uncontrolled blood pressure, uncontrolled blood sugar, smoking, and obesity seem to be among the biggest risk factors for progressing from CKD to dialysis. CKD patients are at higher risk for having a cardiovascular (CV) event, such as heart attack, stroke, or peripheral CV disease.

**Q: For CKD patients who might have a CV event before dialysis, is such an event a complication of the CKD or is it something that comes with other things going on in their lives?**

**A:** It is a co-morbidity or complication of CKD. Now we know they have an increased risk of CV disease if they have CKD. Their atherosclerotic burden—how quickly plaques build up in their arteries—accelerates much faster than that of a person who doesn't have CKD, so they are more likely to have a CV event and to die from it.

**Q: What would you tell a person who has been recently diagnosed with CKD? Do you have words of encouragement for them and possibly their caregivers?**

**A:** Absolutely, we always have to be encouraging and counsel our patients as much as we can. It's much easier when it's early. There have been great initiatives by the National Kidney Foundation and ASN to indicate to the public that patients with kidney disease need to see a nephrologist in the early phases. In the early phases, we can really have an impact in delaying progression.

It's more difficult when that person presents and they are very close to needing dialysis, yet they may not have had symptoms and may have never been told they are close to dialysis before. That is very hard for the patient and for the family. We still need to encourage and educate them that there are very different modalities of dialysis and the technology has improved. We want them to see it as a potential bridge to kidney transplantation because we know once they get a transplant, patients can do very well and lead normal lives.

**Q: You recently published a study in the *Journal of the American Society of Nephrology* that found that people who consumed higher levels of fructose were at higher risk for high blood pressure. Can you explain those results?**

**A:** This is a study that was done with Dr. Diana Jalal and Dr. Rick Johnson. We were able to use data from the National Health and Nutrition Examination Survey (NHANES), a survey done by the CDC every two years with very detailed data on the U.S. adult population, including demographics, dietary habits, and blood pressure of normal subjects. The idea was to establish a relationship between fructose intake and blood pressure level.

The median value of fructose intake was about 74 grams per day, or about two to three cans of regular cola or soda pop drink. We found that the individuals with a higher intake of fructose appeared to have a higher risk of elevated blood pressure. The higher the fructose intake, the higher the blood pressure.

**Q: Why would this relationship exist with fructose but not other sugars like sucrose that we take in through our diet?**

**A:** There are two hypothetical mechanisms. One hypothesis put forward by Dr. Johnson is that fructose may be involved in the control of uric acid. Uric acid levels in blood have been related to death, CV disease, and to kidney disease progression. Too much uric acid is generally bad. Fructose may interfere with the metabolism of uric acid, causing an increase. That will affect the renin angiotensin system (RAS), and may have an effect on elevated blood pressure.

The other potential mechanism is that fructose may stimulate the sympathetic nervous system, causing vasoconstriction of blood vessels, and that could also elevate blood pressure. These properties have not been found for other kinds of sugars.

**Q: The Corn Refiners Association, which represents the makers of high fructose corn syrup, and the American Beverage Association, which represents soda makers, has expressed doubt about these findings, saying there's no clear causal link. How would you respond to that?**

**A:** We make clear in our paper that we cannot establish a causal link. This is just an association. No question when you put all the associative and basic science data that has come out, it has suggested that there is a causal relationship. That's a main limitation of our epidemiology study. However, it's absolutely worth looking into further.

**Q: Can you discuss the relationship between high blood pressure and CKD? Why is hypertension so bad for causing CKD and its progression?**

**A:** The main mechanism is that blood pressure is just putting stress on the vascular bed, and the vasculature is the largest organ that we have. Obviously, the kidneys have a very high blood supply, so everything that is going to happen in the vasculature is going to affect the kidney too.

The interesting thing is that we really do not know in a true interventional trial if blood pressure reduction reduces the risk of new onset CKD or progression to dialysis. The NIH has launched the biggest hypertension and CKD trial, called Systolic Blood Pressure Intervention Trial (SPRINT), with 7500 individuals who will be randomized to two different systolic blood pressure levels, 140 mm Hg versus 120 mm Hg. Close to half of the patients will have true CKD. The question is, does decreasing blood pressure to a certain level really avoid CKD and progression to dialysis? It will also look at death, CV events, and strokes. It is one of the largest hypertension trials that has ever been done and will hopefully start at the end of 2010.

**Q: Just because someone has high blood pressure does not necessarily mean they will develop CKD. Are there ways to predict who will and who won't?**

**A:** That's a great question. There are 68 million adults with hypertension, but only 400,000 on dialysis, and maybe only a quarter of those are due to hypertension. There are tests like the 24-hour blood pressure monitoring. During nighttime we all should experience a dip in our blood pressure. But some patients are non-dippers, and that may be a risk factor for kidney disease progression in hypertensive patients. Uncontrolled hypertension, with bouts of accelerated malignant hypertension with eye changes and chest pain, that's associated with progression of kidney disease as well.

**Q: Why are type 2 diabetics at risk for CKD and what can they do to lower their risk?**

**A:** Kidneys are big filters that normally filter out all the bad substances and keep the good ones. Unfortunately, diabetes causes damage in the glomeruli,

the functional unit of the kidney, which causes the leakage of protein. As you leak protein in larger amounts, it causes scar tissue in the glomerulus, accelerating progression of kidney disease.

This is where the angiotensin converting enzyme inhibitors and angiotensin receptor blockers are important. These drugs were formulated for blood pressure, but as a very good side effect, they also stop the leakage of protein. The data suggest that very early in the course of kidney disease, type 2 diabetics need to be on these medications. Even before microalbuminuria is present, being on these medications may delay potential kidney disease.

**Q: Moving on to the research of other investigators, what do you consider the most exciting research advances in kidney disease today?**

**A:** I think the most exciting advances will come in kidney disease progression and what we can do to delay it. There's fascinating research in this area using anti-fibrotic agents. When disease in the kidney progresses, the kidney scars, so can we reverse the scar to try to improve the kidney function? For example, [some researchers are testing] using a TGF-β antibody medication to prevent scarring and hopefully reduce progression.

In my area of research on mineral metabolism, patients with CKD develop an imbalance in calcium and phosphorus and their bone health. I think there are very important studies of how to best manage this condition. In general, we need more interventional trials. It sounds very simplistic, but as a specialty in medicine, we are behind other specialties in doing well-designed prospective, interventional studies where we can then give the best recommendations to our patients.

**Q: How do you think the recent health care reform measures are going to affect kidney health care professionals?**

**A:** I think it's already affecting us. New Centers for Medicare and Medicaid Services (CMS) guidelines have already come out with bundling of payments for dialysis patients. Dialysis is one of the very few conditions that is paid for by the government, by Medicare, if the patient has no insurance. This is very expensive, it represents about 8 to 10 percent of the total Medicare budget for around 1 percent of the population, so we're talking around $2 billion per year. Medicare has realized that this is a costly procedure and now they have bundled the whole dialysis treatment.

When a patient goes on dialysis, we have the expenses of the physician, the nurse, the technicians, and the medications at the center. Now, Medicare wants to apply one single rate for that treatment, even though the costs might be much higher than the amount given to the dialysis centers by CMS. So now, centers will have a smaller budget to try to keep the same expenses.

There will most likely be little changes in perhaps the way lab tests are done or the way medications are given. All, of course, in keeping with good patient care, we would never compromise good patient care at the expense of costs. But there's no question that the rationing of health care is coming. It has affected our community and the ones who will be affected first are the dialysis patients.

**Q: There are many different dialysis options now. Will those options stay the same with the health care changes or will there be fewer options?**

**A:** Initially, the options will stay the same. There are two large trials looking at the effect of daily dialysis and nocturnal dialysis on the survival of dialysis patients. It's thought that the more dialysis a patient gets, the better. But obviously that would be more costly.

The standard for most patients is three times per week, for four hours each time, for intermittent hemodialysis. There is also now a growing number of nocturnal programs, in-center where patients go for eight hours at night, three times per week. And the question the studies are examining is, what about four or five days? Preliminary data show that the nocturnal patients are doing very well, but what if they need more eight-hour sessions? The cost will be significantly higher than it is now, so the question is what are we going to do at that time? And if more is better, who will pay the bill? But this is really hypothetical now.

**Q: Are there any misconceptions about CKD that you think the public has that you'd like to clear up, or anything else you'd like to tell people about it?**

**A:** When patients hear that they have kidney disease they immediately feel it means they are going on dialysis and that dialysis is a death sentence. Our responsibility as physicians is to educate the public that patients do live normal lifestyles with kidney disease, and even on dialysis and even with a kidney transplant. That it's not a death sentence, there are therapies to try to get patients through the different stages of kidney disease.

Is the diagnosis devastating? Absolutely. But, our therapies do keep patients alive and most of our patients have a very decent quality of life. Those who are able to progress to a kidney transplant have a great quality of life and are able to work and have a routine, normal life. The biggest misconception is that dialysis is like having incurable cancer and I think, with education, that is something we can change.

**Q: Finally, what would you say a professional society like ASN can do to help combat CKD?**

**A:** I think the National Kidney Foundation and ASN have already done a lot of education. ASN was at the forefront of transforming serum creatinine levels into GFR. Now, at most hospitals around the country when a physician is seeing the blood values, right next to the creatinine, it says this is consistent with a GFR of 40. Seeing that rate of GFR is like a red flag to a primary care physician. This has created a lot of awareness around what CKD is and has increased early referrals of patients to a nephrologist. ASN's CKD advisory group was at the forefront of getting this message across, informing, educating, and talking to people about the condition. In my mind, this education is extremely important.

# How do you navigate unprecedented change?

# As a team.

Since the beginning, we've delivered comprehensive testing, analysis, and reporting with the reliability and personal service you require to ensure the best outcomes possible for your patients. **Our trusted team of clinical experts, paired with our patient-centric tools and resources help you comply with new industry guidelines—so you can navigate unprecedented change with the utmost confidence and ease.**

**www.spectra-labs.com**



spectra® laboratories

# Glomerular Disease in the Elderly:
## To Biopsy or Not to Biopsy

By Richard J. Glassock

The spectrum of glomerular diseases that affect the elderly is quite broad and ranges from the relatively benign minimal change disease to fulminant crescentic glomerulonephritis. Postinfectious glomerulonephritis has seen a resurgence in the elderly, whereas its occurrence in younger patients is diminishing, except in resource-poor regions of the world. Some glomerular lesions are distinctly more common in the elderly than in younger adults, such as primary (AL) amyloidosis, nonamyloid monoclonal immunoglobulin deposition diseases (e.g., light chain deposition disease), antineutrophil cytoplasmic antibody (ANCA)-associated small vessel vasculitis (SVV), and diabetic glomerulosclerosis (consequent to type 2 diabetes mellitus).

The performance of a percutaneous renal biopsy may provide crucial diagnostic and/or prognostic information in many patients suspected of having a glomerular lesion based on clinical or laboratory examinations. There is no evidence that the risk of complications from a renal biopsy procedure is any greater in the elderly than in younger adults, providing the usual precautions are taken and the procedure is conducted by an experienced practitioner. Thus, the decision to perform a renal biopsy in an elderly patient is often guided by three questions: 1) Will the information gained provide useful diagnostic value (i.e., will it reduce uncertainty of diagnosis)? 2) Will the information gained be helpful in designing a safe and effective treatment strategy, even if the diagnosis is reasonably secure? 3) Will additional prognostic information not already obtainable by noninvasive clinical and laboratory testing be forthcoming?

The decision to perform a renal biopsy will depend on how these questions are answered. It will also depend to a certain extent on the *a priori* estimates of the probability of the presence of certain disease states or entities. For example, an elderly patient with clinical features of nephrotic syndrome, impaired renal function, cardiomyopathy, carpal tunnel syndrome, orthostatic hypotension due to autonomic neuropathy, and elevated plasma-free lambda light chain concentration may not require a renal biopsy to confirm the presence of AL amyloidosis—an abdominal fat pad biopsy/aspiration may suffice. Renal tissue would not be helpful in designing a safe and effective treatment strategy, and most of the useful prognostic information is already contained in the clinical examination. On the other hand, an elderly patient presenting with the recent onset of an apparently "idiopathic" nephrotic syndrome and normal or only mildly impaired renal function would benefit greatly from the diagnostic precision afforded by a renal biopsy.

Were membranous nephropathy (MN)— one of the most common lesion seen in elderly patients with nephrotic syndrome (Table 1)—to be discovered, a sequence of additional studies would be initiated to exclude a secondary cause, most notably an underlying occult malignancy that can be present in as many as one in four or five elderly patients with MN. If a secondary cause is not found, the morphologic features of the MN lesion do not provide much aid in choosing a course of treatment or offering a more precise estimation of prognosis, over and above that enabled by clinical information (such as serum creatinine levels or urinary protein excretion rates).

One of the more common and often devastating glomerular diseases seen in the elderly is ANCA-associated crescentic glomerulonephritis (a form of SVV that is either renal-limited or multisystemic). In this circumstance, serological tools (antigen-specific [ELISA] anti-myeloperoxidase auto-antibody and anti-proteinase-3 auto-antibody and ANCA testing by indirect immunofluoresence) are readily available to render a diagnosis with high precision, even in the absence of a renal biopsy. However, the degree of crescent formation (e.g., the percentage of well-preserved [normal] glomeruli) and the extent of tubulo-interstitial fibrosis and tubular atrophy may provide information that helps generate a treatment strategy and refine the prognosis, provided that the sample size is adequate (at least 15–20 glomeruli). However, the prospect of gleaning additional information from a renal biopsy in these cases should not delay the initiation of treatment based on clinical information alone.

The utility of renal biopsy in elderly patients with type 2 diabetes mellitus and concomitant overt proteinuria with or without impaired renal function is especially difficult to determine. Most of these patients will have an underlying diabetic glomerulosclerosis (diffuse or nodular intercapillary glomerulosclerosis), and renal biopsy will not aid in diagnosis, treatment, or prognosis. However, a fraction (5–40 percent, depending on the clinical details) will have another nondiabetic glomerular lesion or one superimposed on a background of diabetic glomerulosclerosis. Recently, postinfectious glomerulonephritis with underlying immunoglobulin A–dominant glomerular deposits has been observed in elderly individuals with diabetes.

Identification of the underlying lesion can have a decided effect on treatment and/or prognosis. Clinical clues to the presence of a nonglomerular lesion in elderly patients with type 2 diabetes and overt signs of renal disease include 1) an onset of renal manifestation after only a short duration of recognized diabetes (which is often difficult to establish due to the delay in diagnosis of type 2 diabetes); 2) the presence of an "active" urinary sediment, including red cell casts and/or acanthocytes; and 3) deterioration of renal function at a pace exceeding that usually seen in type 2 diabetes with overt diabetic nephropathy. The absence of diabetic retinopathy is much less useful in enhancing suspicion of a nondiabetic glomerular disease in individuals with type 2 diabetes compared with those with type 1 diabetes. As a general rule, it is better to recommend a renal biopsy (extant contraindications) in cases of type 2 diabetes with an "atypical" presentation of overt renal disease. There are no compelling reasons to recommend a renal biopsy in patients with microalbuminuria and type 2 diabetes.

Amyloidosis, MN, ANCA-associated SVV, and diabetic nephropathy illustrate the complexities involved in determining the overall efficacy of renal biopsy in elderly individuals suspected of having an underlying glomerular disease. In some instances, it is critically important to obtain a correct diagnosis, and renal biopsy may be the only certain way of achieving this goal. In other circumstances, the diagnosis can be established with reasonable certainty via noninvasive clinical examination and well-selected laboratory testing (including imaging). Here the value of renal biopsy rests mainly in the prognostic arena in both a positive and negative sense—implementing specific treatment using evidence-based guidelines when the lesion appears to be modifiable and rendering conservative (i.e., palliative) nonspecific management when the lesion appears to be nonmodifiable. Therefore, the decision to biopsy or not to biopsy is a complicated one that can only be made on a case-by-case basis after consideration of all of the clinical information available (history, examination, laboratory, and imaging). Because renal biopsy is a reasonably safe procedure, in experienced hands, it may be better to err on the side of commission than omission when uncertainty might affect the outcome of a disease process. One should always keep in mind that glomerular lesions occur more commonly in the elderly (Table 1) when applying this principle. In this context, it is also important to be thorough in the application of an ever-enlarging array of noninvasive diagnostic and prognostic tools (e.g., serology) in this group of patients. In many cases, renal biopsy may not be an essential part of the evaluation and management of elderly patients with clinically overt glomerular disease.

**Table 1. Common glomerular lesions in the elderly**

- Primary and secondary amyloidosis
- Monoclonal immunoglobulin deposition diseases
- Membranous nephropathy
- ANCA-associated crescentic glomerulonephritis
- Diabetic glomerulosclerosis (type 2 diabetes mellitus) with or without superimposed nondiabetic glomerular disease
- Postinfectious glomerulonephritis

**Suggested reading**


1. Bomback AS, et al. ANCA-associated glomerulonephritis in the very elderly. *Kidney Int* doi: 10.1038/ki.2010.489.
2. DiPalma AM, et al. Kidney biopsy in the elderly. *J Nephrol* 2010; 23: s5–s60.
3. Glassock RJ. Glomerular disease in the elderly. *Clin Geriatric Med* 2009; 25:413–422.
4. Mohamed N, John R. Use of renal biopsy in the elderly. *Int Urol Nephrol* doi: 10.1007/s11255-010-9874-9.
5. Nasr SH, et al. Postinfectious glomerulonephritis in the elderly. *J Am Soc Nephrol* doi: 10.1681/ASN.2010060611.
6. Pincon E, et al. Renal biopsies after 70 years of age: a retrospective longitudinal study from 2000 to 2007 on 150 patients in Western France. *Arch Gerontol Geriatr* 2010; 51:e120–124.


*Richard J. Glassock, MD, is emeritus professor of medicine at the Geffen School of Medicine at the University of California Los Angeles.*