ASN LEADING THE FIGHT AGAINST KIDNEY DISEASE

KidneyNews

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The IOM on Salt—Is Too Little the Same as Too Much?

By Kurtis Pivert

A new report on sodium and health found recent evidence is insufficient to support recommended dietary intake levels. The Institute of Medicine (IOM) analysis—*Sodium Intake in Populations: Assessment of Evidence*—has ignited a debate about whether salt restriction is linked to health benefits, especially for at-risk individuals (1).

Recent studies selected by the IOM offered inconsistent or insufficient evidence that a daily sodium intake of 1500 mg (for certain patient subgroups) or 2300 mg (for the general population) reduced the risks of cardiovascular disease or premature mortality.

The IOM also concluded that a two-tiered approach to sodium intake—one recommended level for patient subgroups and another for the general population—was not warranted. Patient subgroups included those 51 years or older, African Americans, and individuals with kidney or cardiovascular disease, diabetes, or hypertension.

Discussion has centered on the narrow focus stipulated by the Centers for Disease Control and Prevention (CDC), which commissioned the review. The IOM excluded literature using surrogate markers, namely blood pressure, concentrating instead on studies using direct health outcome end points. Yet the relevance of this evidence has been questioned over unconventional clinical approaches or methodological limitations. Because of the contentious reaction, the authors felt it necessary to clarify their findings in a recent *JAMA* article (2).

Although affirming the association between higher sodium intake and increased cardiovascular risk, the report's remaining conclusions conflict with current dietary guidelines and contradict the IOM's previous recommendations on sodium and health (3,4). Its publication comes as Americans' addiction to salt remains undiminished, with average consumption holding steady at 3400 mg/day in spite of multiple initiatives to reduce excessive intake.

To understand the controversy surrounding the IOM's findings, *ASN Kidney*

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Ultrasound Therapy May Help Prevent and Treat Acute Kidney Injury

By Tracy Hampton

Acute kidney injury is one of the most common and serious complications of hospitalized patients. Yet there are no FDA-approved therapies for this disorder except dialysis, and potential drug therapies are associated with a number of adverse effects.

"There is an important gap in our ability to address this problem," said Mark Okusa, MD, of the University of Virginia. Okusa and his colleagues may have stumbled upon a solution when they unexpectedly discovered that ultrasound exposure provides a simple, portable, noninvasive, and nonpharmacological approach to prevent acute kidney injury and long-term kidney fibrosis. Their findings were published recently in the *Journal of the American Society of Nephrology*.

Ultrasound alone

Working with Joseph Gigliotti, PhD, also of the University of Virginia, and others, Okusa has been developing an ultrasound-based method to deliver drugs specifically to the kidney to prevent or treat ischemia-reperfusion injury. This type of injury contributes to tissue damage and reduced glomerular filtration rate in some patients who undergo major surgery, which can deprive the kidneys of normal blood flow. In addition to de-

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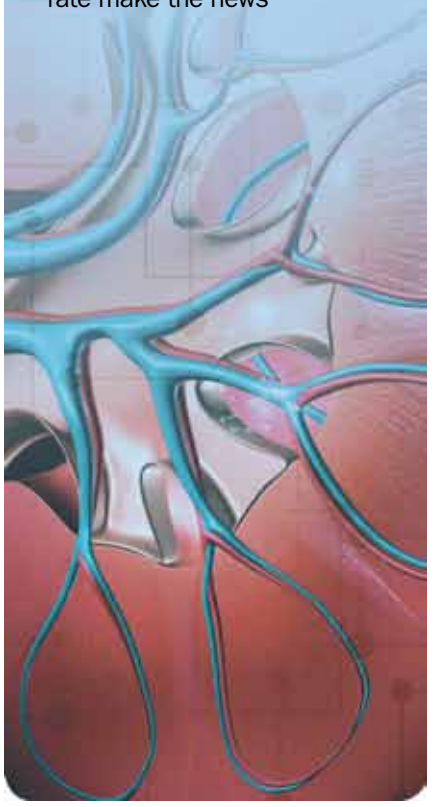

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Ultrasound Therapy

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veloping after procedures such as kidney transplantation and cardiopulmonary bypass, renal ischemia-reperfusion injury contributes to the main pathophysiological processes that occur during sepsis-contrast- and rhabdomyolysis-induced kidney injuries.

In the researchers' approach, they package a drug in a "microbubble" that is injected into a laboratory animal. When the drug-loaded microbubble enters into the kidney, ultrasound is used to break up the bubbles, thereby releasing the drug and enhancing its delivery to the kidney.

Through careful experiments, the research team was surprised to find that ultrasound alone—without drug-laden microbubbles—protected the kidney from ischemic injury. When the investigators exposed anesthetized mice to ultrasound with a routine clinical imaging system 24 hours prior to blood disruption to the kidneys, the mice exhibited preserved kidney health after blood flow was restored. In contrast, sham-treated mice exhibited significant kidney injury.

Also, ultrasound treatment reduced the infiltration of immune cells that typically occurs in the kidney after ischemia-reperfusion injury, and it caused a greater than 85% reduction in the renal expression of vimentin, α-smooth muscle actin, collagen I, and collagen III mRNA.

Ultrasound treatment prevented the marked decline in kidney function as well as tissue injury, and it also protected the kidneys from subsequent development of fibrosis. The regimen relied on settings within approved Food and Drug Administration guidelines, and the protective effect of a single exposure lasted for two days.

Mechanism of action

Additional experiments—including splenectomies and adoptive transfer studies—revealed that the ultrasound treatment blocked ischemia-reperfusion-induced kidney inflammation through direct action on the spleen, an organ that appears to modulate the response to acute kidney injury. Blockade or genetic deficiency of the α7 nicotinic acetylcholine receptor abolished the protective effect of ultrasound, suggesting the involvement of the cholinergic anti-inflammatory pathway, which mediates the neural control of systemic inflammation.

"Our studies using noninvasive ultrasound now provide us with an active treatment that appears to be simple, effective, and nontoxic for the prevention of acute kidney injury," said Okusa. "To our knowledge this has never been described for the prevention of tissue or organ injury. Interestingly, we suspect that similar mechanisms that lead to kidney injury may also lead to lung, heart, and liver damage and that this form of therapy might be effective for prevention of injury in other organs as well."

Future analyses will explore the efficacy of ultrasound in reducing mortality in subjects with more severe kidney injury, perhaps from longer ischemic times. Also, research is needed in larger animals and then humans to apply the concepts learned from this study. Finally, the current study only addresses preventive therapy, and it is unclear whether this form of therapy is effective as a treatment after injury occurs.

In an accompanying editorial, Alain Le Moine, MD, PhD, of the Erasme Hospital in Belgium, and his colleagues noted that opportunities arising from the work are numerous and promising because many procedures that carry a very high risk of AKI are planned.

"In searching for novel approaches to prevent and even cure acute kidney injury, we believe that splenic ultrasound stimulation has a bright future ahead," they wrote. They also noted that other nonrenal conditions—such as myocardial ischemia, hepatic injury, sepsis, and endotoxemia—also rely on the cholinergic anti-inflammatory pathway and might therefore be prevented or treated with the approach.

Study co-authors include Liping Huang, Hong Ye, Amandeep Bajwa, PhD, Kryt Chattrabhuti, MD, Sangju Lee, MD, Alexander Klibanov, PhD, Kambiz Kalantari, MD, MPH, and Diane Rosin, PhD.

Mark Okusa has the following disclosures: AM Pharma, Nature Publishing Group, Lilly, Daiichi-Sankyo, American Physiological Society, International Society of Nephrology, PGX Health/Adenosine Therapeutics, LLC, and UVA Patent Office.
Alexander Klibanov has the following disclosures: Targeson, Inc, Philips Research.

The article, entitled "Ultrasound Prevents Renal Ischemia-Reperfusion Injury by Stimulating the Splenic Cholinergic Anti-Inflammatory Pathway," is available online at http://jasn.asnjournals.org/.

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IOM on Salt

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News spoke with several outside experts about the scope of the review, and the methods and evidence behind its conclusions. These specialists—from nephrology, internal medicine, nutrition, and cardiology—gave their perspectives on how the report and current research may influence physicians' clinical approach to patient care. Lastly, they identified knowledge gaps on sodium's effects on health, in the general and kidney disease populations, that require further research.

An emphasis on direct health outcomes

Although literature has shown that decreasing sodium intake can reduce blood pressure, the CDC wanted to determine if salt restriction could influence the risk for adverse health effects. The agency asked the IOM to evaluate studies investigating the effects of sodium restriction on health published since the institute's 2005 report on dietary intake (5).

A 12-member committee—including experts in epidemiology, nutrition, hypertension, and nephrology—examined the health effects of restricting sodium in the general population and patient subgroups. Unlike previous reviews, the IOM only included literature reporting on the direct health effects of reduced sodium intake (e.g., cardiovascular events or premature death), and only reviewed evidence published after the prior report.

"The IOM's narrow charge excluded studies investigating the effects of reduced intake on blood pressure, a key determinant of health and the largest determinant of preventable mortality worldwide," said Lawrence Appel, MD, an internist and director of the Welch Center for Prevention, Epidemiology and Clinical Research at Johns Hopkins University.

John Forman, MD, MSc, a nephrologist at Harvard Medical School, agreed. "They left out some important studies by removing blood pressure as a serious health outcome."

Instead the committee focused only on a piece of the evidence linking salt to health outcomes. "There are two huge problems with these types of studies," said Appel. "The first is very poor measurements of sodium intake. The second is reverse causality, which is a particular problem with studying kidney disease."

Because patients with chronic kidney disease (CKD) are less physically active and consume fewer calories (the most significant determinant of sodium intake) they consume less sodium as the disease progresses. "The directionality is the disease reducing sodium not reduced sodium causing the disease," Appel said.

"The focus on outcomes instead of biomarkers is a key question in biomedical research right now," said Scott Hummel, MD, a cardiologist and researcher at the University of Michigan. "Depending on the population, hard outcome–based studies are often lengthy and costly, but previous instances have shown they can turn conventional wisdom on its head."

Diverse study methodologies and populations prevented the committee from conducting a formal meta-analysis. Instead, papers were evaluated for generalizability and risk of bias. Of 200 articles initially reviewed, 38 were included in the report. The majority investigated cardiovascular disease and stroke (25 studies) followed by gastrointestinal cancer (eight), with only two studies each on kidney disease, metabolic syndrome, and diabetes.

Inconclusive and inconsistent evidence on health risks

The selected evidence confirmed the positive relationship between high dietary sodium intake and increased cardiovascular risk. Yet the same studies offered inconsistent or insufficient evidence that restricting intake to less than 2300 mg/day has either positive or negative health effects.

The American Heart Association and Academy of Nutrition and Dietetics were among the organizations disagreeing with the IOM, both reiterating that daily sodium intake should not exceed 1500 mg. Unsurprisingly, the Salt Institute hailed the report, stating "there is no scientific justification for population-wide sodium reduction to such low levels."

Reaction among the experts interviewed for this article was mixed. Harvard's Forman found the conclusions unexpected, "especially given the 2010 IOM report (4) suggesting that sodium reduction was a key component to reducing the population burden of hypertension."

"Their charge was to look at a set of evidence—cohort studies and observational studies—which are a very tricky form of evidence to interpret," said Appel. "I'm a little bit surprised they used that evidence to question sodium levels, but in some respects I'm not because that was what they were assigned to review."

Others anticipated the report's findings. "I was not surprised because there are a minimal number of studies looking at hard outcomes and sodium restriction," said Hummel.

Pamela Singer, MD, a pediatric nephrologist at Montefiore Medical Center in the Bronx, NY, noted "much of the recent literature supports the J curve model, where the risk for adverse health effects is greatest at the highest and lowest ends of sodium intake." Changes in renin-angiotensin and triglycerides or insulin resistance can occur with very low sodium levels, and all these factors have to be taken into account when assessing cardiovascular risk, she said.

But Appel, lead author of the DASH (Dietary Approaches to Stop Hypertension) study (6) noted that in the study "a reduction in sodium to 1500 mg/day had no effect on LDL cholesterol and other lipids."

The IOM cautioned the unconventional clinical approach in several studies from one group differed greatly from U.S. care standards and thus may not be generalizable. Several experts contacted for this article also raised concerns about these studies' unorthodox methods, including regimens of high doses of diuretics concurrent with fluid restriction. Uncertainty about this evidence was heightened after a meta-analysis including two of these papers was retracted "on the ground that the reliability of the data on which it is based cannot be substantiated (7)."

Population-based intake recommendations

The IOM found no health benefits, and instead the potential for adverse health outcomes, by restricting daily sodium intake to between 1500 mg and 2300 mg for patient subgroups—particularly those with CKD, diabetes, and cardiovascular disease. They also concluded evidence did not support treating patient subgroups differently from the general population.

"In aggregate these high-cardiovascular-risk groups comprise a majority of the U.S. population, which is a disturbing statement," said Hummel, "but that doesn't mean the response to sodium restriction will be similar in all subgroups." He observed that dietary modification research is inherently challenging. "It's hard to measure intake, gauge adherence to dietary recommendations, and sustain adherence over time."

From a population perspective it's easier to have one goal instead of a two-tiered approach, said Appel, but evidence for the lower intake goal is based on blood pressure studies excluded by the IOM. "There is strong evidence that middle-aged and older adults and African Americans are especially sensitive to the blood pressure–lowering effects of sodium reduction. In fact, sodium reduction has tremendous potential to reduce racial disparities in blood pressure–related cardiovascular disease," he said.

Target ranges for dietary sodium were not requested by the CDC.

Sodium effects on the kidney

Only two of the 38 studies examined the effects of sodium restriction on the kidney. One was a post-hoc analysis (Heerspink et al.) of two well-performed large randomized trials of diabetic nephropathy that measured sodium intake by a 24-hour urine collection, Forman said. "It showed that low sodium intake was associated with a lower rate of adverse events (compared with a higher sodium intake) among those patients taking an angiotensin receptor blocker (ARB)."

"Yet the IOM failed to include another post-hoc analysis of the REIN (Ramipril In Non-Diabetic Renal Failure) randomized trial (which included patients with non-diabetic kidney disease) that showed similar results (although patients received angiotensin-converting enzyme [ACE] inhibitors rather than ARBs) (8)," said Forman. Another study missed by the IOM—McCausland and colleagues' post-hoc analysis of the HEMO randomized trial—found a high sodium intake in hemodialysis patients was associated with increased mortality (9).

"Thus, in patients with both diabetic and nondiabetic renal disease receiving angiotensin inhibition, these studies suggest that patients who consume less sodium have better outcomes," Forman said. "Since most nephrologists will treat their patients who have diabetic and nondiabetic kidney disease with either ACE inhibitors or ARBs, the evidence (although observational) suggests that a low sodium diet is better."

Although omitted from their analysis, the IOM surveyed research reporting proteinuria and renin-angiotensin-aldosterone system (RAAS) biomarkers. Increasing proteinuria due to increased sodium consumption was linked to CKD progression.

"Most of the studies on proteinuria are consistent—the more salt you consume, the more proteinuria you have," said Appel. "I think there's a reasonable case to be made for lower salt intake in kidney disease, but acknowledge the need for more evidence."

Evidence using the RAAS biomarker was less conclusive, with reduced sodium levels increasing plasma renin activity (PRA), a proposed predictor of cardiovascular disease. "PRA goes up when blood pressure or blood volume goes down, it's a counterregulatory response," said Appel. "Some believe it's an important biomarker, but it's a risk correlative, it's not causal." He pointed to the Yonomami Indians in Brazil who consume little salt, have high PRA levels, but very little vascular disease (10), and the ALLHAT (The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial) where a diuretic arm (which raises PRA) and ACE inhibitor arm (which lowers PRA) experienced similar cardiovascular outcomes.

Reducing sodium in processed foods

The same week the IOM report was released, *JAMA Internal Medicine* published a study of sodium content in processed and restaurant foods—the source of almost 80 percent of sodium consumed in the United States. The authors concluded government regulation of sodium was needed after finding minimal declines after voluntary industry reduction measures (11).

Sodium content in processed foods and fast-food items was tracked over a 6-year period. Levels in processed food declined 3.5 percent but increased 2.6 percent in restaurants, with individual products varying up to 30 percent.

However, reducing sodium levels creates new problems. "Phosphorus is a big concern," said Lauren Graf, MS, RD, a renal dietician at Montefiore Medical Center. "Many low-sodium processed foods are high in phosphates, which are added as a preservative and can be more harmful, especially to patients on dialysis."

Since industry and government efforts have failed to lower sodium consumption, what could reduce the excessive intake levels in the United States?

Education could make the difference, suggested Singer. Knowing which foods are highest in sodium—such as bread—could help people make informed choices.

Graf said a broader approach was needed, stating that government initiatives focusing only on sodium reduction miss the mark. "The goal should be increasing intake of whole foods, fruits, and vegetables that are naturally lower in sodium and higher in fiber, antioxidants, and minerals, such as potassium, that can help lower hypertension." The *JAMA Internal Medicine* article examined only one nutrient, but the foods analyzed

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were high in transfats, saturated fat, refined carbohydrates, and chemicals. "Even if the sodium content were reduced, there wouldn't be much health benefit," she said.

A change in clinical approaches

Could the IOM report influence physicians' clinical approach to treating patients with hypertension or kidney disease?

Hummel didn't think so. "The importance of sodium restriction is so ingrained in medical practice, which is a separate question from whether sodium restriction is a good idea," he said. "It will take more than the IOM report to change practice."

Nevertheless, Forman believes the report and press surrounding it could likely reduce concerns about sodium intake among nephrologists and patients with kidney disease. "This is unfortunate, especially given the way the IOM considered the data."

For renal dieticians it depends on the patient.

"Low sodium intake is still recommended for patients on dialysis, but the IOM report could change the way that dieticians counsel patients with hypertension or early stages of CKD," Graf said.

Although pediatric nephrologists regularly encounter hypertension, one concern with excessive sodium restriction in this population is the potential for adverse consequences on growth, said Singer. "Sodium is an essential electrolyte, and children need that to grow."

A need for more research

The IOM found the literature was limited by methodological approaches, particularly with evaluating sodium intake, and recommended further research including the health effects of sodium in combination with other electrolytes, and interactions with antihypertensives and sodium restriction on blood pressure.

Graf said future studies should look at the broader picture, including such factors as obesity and other nutrients and not just sodium intake. "The dietary aspects of cardiovascular disease are multifactorial, and we can't just look at one single nutrient," he said.

Appel noted that despite very good evidence linking salt intake and proteinuria, more research on salt and blood pressure in kidney disease is needed.

"Although randomized controlled trials are viewed as the gold standard, in this case the most useful studies are prospective observational studies evaluating multiple effects of sodium intake over time because they are more reflective of reality," said Singer.

Yet Forman thinks one or more randomized trials are needed because the evidence reviewed by the IOM was observational. "Patients in the trial should have non–dialysis dependent CKD, and the end points should be ESRD and death," he said.

Hummel suggested research into biomarkers and better measurements of sodium intake. "A biomarker of salt sensitivity that could predict blood pressure response to sodium changes, but more importantly could be associated with a mechanism for cardiovascular disease or CKD, would be ideal," he said.

And although 24-hour urine collection is the gold standard, there are problems with incomplete urine collections, and something that could reduce the complexity, such as a spot urine sample, would be beneficial."

It may be difficult to move this research forward, however. The spending cuts mandated under sequestration have contracted available research funding, and it remains unknown what alternate funding sources may be available to support this science.

Singer believes they'll be funded, especially given the overall cardiovascular burden in the U.S. health care system.

Kidney disease is a tough area to get research funded, said Appel.

"The right studies can be expensive studies ($25,000 per person or more for a feeding study), and this is a bad climate for such research," he said. "It's going to take a change of mindset among funding agencies to fund the right kind of studies that yield high-quality results that can be used to form guidelines."

Hummel noted that previous studies have suffered from the preconception that sodium's effects on health were established.

"The more studies that come out about the uncertainty in this area will help with future funding, not just in a population perspective but also high-risk subgroups."

Despite the debate surrounding the IOM's conclusion on lower sodium levels, the report confirms the dangers of excess sodium consumption for health. Americans' reliance on high-sodium processed and restaurant foods—42% of each food dollar is spent outside the home (11)—and steady thirst for salt raise concerns

about a potential increase in the burden of kidney and cardiovascular disease. Underscoring the need for more research into sodium and health, Hummel concluded "there are huge public health implications for these questions."

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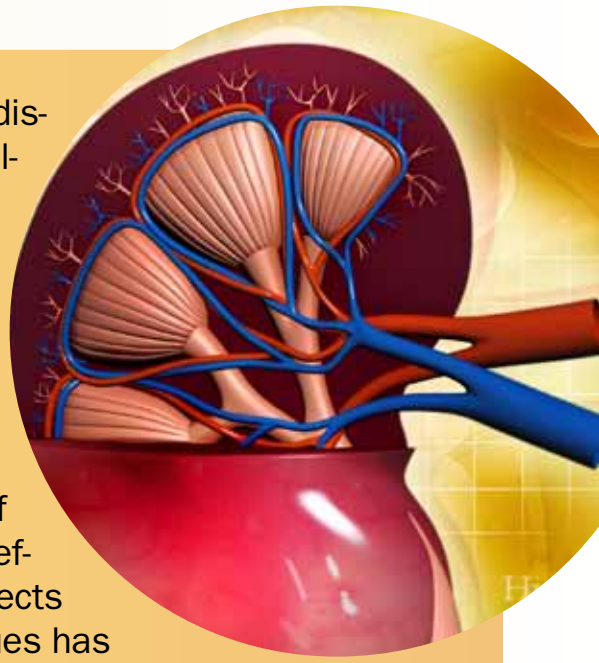
Renal Imaging



In this issue of *ASN Kidney News* we have gathered five articles that briefly discuss hot topics in renal imaging. Imaging is changing rapidly with newly developing hardware and software. This change is being driven by the accelerating pace of sophistication of computers, which form the backbone of radiology and are needed to process the advanced imaging algorithms. Renal function and structure are being examined at the molecular level, which are thereby resulting in more minimally invasive procedures and thus improved accuracy. Concerns about radiation exposure are being addressed with lower dose computed tomography (CT) scan protocols and by maximizing the utility of magnetic resonance imaging (MRI). The combination of new MRI sequences and the lack of necessity for contrast administration has reduced many of the concerning side effects in patients with renal disease and eliminated the lengthy discussion of effects associated with long-term radiation exposure. The advent of these new techniques has allowed radiologists to assist nephrologists in improving the care of their patients without sacrificing diagnostic accuracy. The following articles will introduce you to the latest techniques in renal imaging with attached references for further academic inquiry.

Sandip Patel, MD, and David Wymer, MD, FACNM, FACR, editors of this special section, are affiliated with the Department of Radiology at the University of Florida in Gainesville, FL.

Review of PET/CT in the Diagnosis of Clear Cell Renal Cell Carcinoma Utilizing Radiolabeled Monoclonal Antibodies

By Eric Middlebrooks

The characterization of renal masses, particularly into the benign or malignant category, remains difficult despite advances in computed tomography (CT) and magnetic resonance imaging (MRI) technology, mostly owing to the low specificity of these modalities. Renal cell carcinoma (RCC) is overwhelmingly the most common primary malignancy of the kidney. The typical histologies include clear cell, papillary, and chromophobe.

The majority are of the clear cell histology (ccRCC), accounting for approximately 80 percent of cases (1). Clear cell RCC carries a much less favorable prognosis than papillary or chromophobe (2). Positron emission tomography (PET) utilizing ^{18}F fluorodeoxyglucose (^{18}F-FDG) has had an increasing role in the characterization, staging, and surveillance of numerous malignancies. The role of ^{18}F-FDG PET in characterization of renal masses is limited due to inconsistent tumor uptake. A recent prospective study of ^{18}F-FDG PET in RCC showed a sensitivity of 46.6 percent and a specificity of only 66.6 percent (1).

An investigational PET agent is currently concluding phase III trials using a chimeric antibody cG250 (girentuximab) which is labeled with ^{124}I (^{124}I-girentuximab). The antibody binds specifically with a cell-surface antigen of carbonic anhydrase IX (CAIX) (3).

The CAIX protein is a cellular pH regulator that is normally only expressed in gastric, small bowel, and biliary duct epithelial cells. CAIX is thought to be a player in tumor progression, possibly due to its essential role in pH regulation under hypoxia. The overexpression of CAIX has been seen in multiple cancers including those of ovarian, colorectal, lung, brain, bladder, and renal origins. The most consistent tumor with CAIX overexpression is ccRCC occurring in over 95 percent (1).

Study data from the ^{124}I-girentuximab phase III trial—known as REDECT (REnal Masses: Pivotal Study to DETECT Clear Cell Renal Cell Carcinoma with Pre-Surgical PET/CT)—were recently published and are promising. The multicenter study shows significantly higher sensitivity and specificity of ^{124}I-girentuximab PET/CT compared to both contrast-enhanced CT (CECT) and, although not evaluated directly in the trial, ^{18}F-FDG PET.

The ^{124}I-girentuximab PET/CT sensitivity was 86.2 percent, compared to 75.5 percent and 46.6 percent with CECT and ^{18}F-FDG PET, respectively. More importantly, the specificity of ^{124}I-girentuximab PET/CT for ccRCC was 85.9 percent, compared to 46.8 percent and 66.6 percent for CECT and ^{18}F-FDG PET, respectively.

Although the study was not intended to investigate the size threshold, the sensitivity of ^{124}I-girentuximab PET/CT was 70.8 percent for lesions less than 2 cm and 89.4 percent for lesions 2 to 4 cm. The sensitivity of PET/CT for T1a and T1b ccRCC lesions was 82.8 percent and 95.7 percent, respectively.

Imaging with PET/CT utilizing ^{124}I-girentuximab shows promising results in the evaluation of solid renal masses and specifically in the diagnosis of ccRCC. The exact clinical role is yet to be established for this new agent. Potential applications include improved preoperative staging, including extent of metastatic disease, in patients undergoing resection. The ability to exclude the typically more aggressive ccRCC histology in patients who have multiple comorbid conditions and are poor surgical candidates may show more benefit to watching rather than operating. Also, obviating the need for high-risk biopsy could reduce the morbidity and mortality of diagnosis.

Eric Middlebrooks, MD, is affiliated with the Department of Radiology at the University of Florida in Gainesville, FL.

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Table 1. Sensitivity and specificity of ^{124}I-girentuximab PET/CT compared with other common modalities

Modality	Sensitivity	Specificity
^{124}I-girentuximab PET/CT	86.2%	85.9%
^{18}F-FDG PET	46.6%	66.6%
CECT	75.5%	46.8%

Abbreviations: CT= computed tomography; FDG = fluorodeoxyglucose; PET = positron emission tomography.

Cryoablation of Small Solid Renal Tumors

By Wesley Mann

Over the past decade minimally invasive techniques such as cryoablation, radiofrequency ablation (RFA), and even newer techniques such as microwave ablation have demonstrated efficacy in the management of small renal cancers. These strategies are particularly essential in patients with a solitary kidney or multifocal tumors. This often involves a multidisciplinary effort, particularly in patients with small cancers who are high-risk surgical candidates. Cryoablation is the preferred interventional radiology technique for ablating solid renal masses less than 4 cm. The use of both RFA and cryoablation is supported by current urologic guidelines and represent the state of the art in modern clinical practice (3,4).

The past decade has seen advances in nephron-sparing strategies in the management of solid renal masses ranging from imaging surveillance to open or laparoscopic partial nephrectomy. The proliferation of advanced medical imaging has led to an increased number of asymptomatic cancers diagnosed at an early stage facilitating such conservative management. There has also been a concurrent improvement in 5-year survival rates in this subset of patients despite a rising incidence of renal cancers nationwide (2). While to some degree this increased survival is related to discovery time bias, it is generally agreed that earlier diagnosis and treatment of early cancers increases overall survival.

Open or laparoscopic partial nephrectomy is currently the preferred treatment of T1a disease in otherwise healthy patients. According to current American Urological Association guidelines, ablative therapies including RFA and cryoablation are currently indicated for the treatment of T1a (less than 4 cm) solid renal masses in patients who are poor surgical candidates usually either due to severe underlying cardiac or pulmonary disease (3). It is also recommended that a biopsy be performed concurrent with and immediately prior to the ablation mainly due to the fact that 20 percent of suspicious solid renal masses prove to be benign (3). Additionally, establishing tumor type and histological grade is essential for estimating tumor aggressiveness and establishing prognosis.

Cryoablation involves placing multiple 13- to 17-gauge probes either under laparoscopic, computed tomography (CT), or ultrasound guidance directly into the tumor. Argon or helium gas is used to cool the probes inducing tumor cell death. Usually two freeze–thaw cycles are employed. The procedure can be performed using conscious sedation; however, in the author's experience anesthesia support is often extremely useful. The most common major urologic complication related to cryoablation is hemorrhage (5,6). Other potential complications include thermal injury to the collecting system inducing stricturing and obstruction. The major complication rate for cryoablation is 4 to 5 percent (5,6). Advantages of cryoablation over RFA are a lower risk of urothelial injury and lower risk of incomplete ablation due the heat sink phenomenon, which limits RFA. Imaging surveillance is essential after any ablative therapy.

Current standards of care in the management of patients with selected renal cancers seek to provide oncologic control rivaling traditional radical nephrectomy while avoiding unnecessarily sacrificing functional nephrons leading to chronic kidney disease (CKD) as well as reducing the morbidity and mortality of standard surgery in these patients related to increased rates of systemic atherosclerotic disease processes known to correlate with CKD.

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Dose Reduction Techniques in CT Scanning

By Jacob Batson

Over the past several years, there has been increased emphasis on reducing patient radiation doses, highlighted by the concept of ALARA. ALARA, which means "As Low As Reasonably Achievable," refers to lowering the radiation exposure as much as possible while maintaining diagnostic accuracy. In regards to computed tomography (CT), one method for reducing patient radiation dose is the use of Adaptive Statistical Iterative Reconstruction (ASIR) postprocessing technique. This technique has become a relatively standard procedure and is increasingly accepted in areas such as CT use with children, in which the goal is to balance diagnostic accuracy with that of cumulative radiation dose.

Historically, the most common method of post-CT image processing is the Filtered Back Projection (FBP) technique. However, this method resulted in increased noise in the image sets and hence reducing readers' confidence in diagnostic accuracy of the images. On the contrary, ASIR techniques have the potential to reduce patient radiation doses while increasing the signal-to-noise ratio, and thus improving imaging quality and diagnostic accuracy. Recently, many studies have been published in which a combined ASIR/FBP technique was used to reduce patient dose.

In the adult population, this discussion is highly applicable in patients with recurrent urolithiasis. These patients often undergo multiple CT examinations in follow-up of their renal stone disease, and a relatively high percentage of the patients are young adults who are more susceptible to potential long-term deleterious effects of radiation. In October 2012, Kulkarni and coworkers published a study in *Radiology* comparing radiation doses and the radiologist's diagnostic confidence between noncontrasted renal stone follow-up CT using a full FBP technique, which was their normal protocol for CT, and a modified protocol using FBP/ASIR techniques (1). They reported an approximately 80 percent reduction in radiation dose using the modified protocol with ASIR as opposed to the full FBP protocol with no loss in reader confidence in diagnostic accuracy. In fact, the image quality of the combined ASIR/FBP studies was rated higher. Several similar studies have been published recently in the radiology literature demonstrating that diagnostic quality is maintained or improved using modified ASIR techniques while simultaneously significantly reducing patient dosages.

In recent years, the limiting factors in the widespread use of ASIR techniques were postprocessing computing time and power resource requirements, both of which were substantially increased as more ASIR was used in postprocessing. However, recent advances in imaging software and hardware have reduced the postprocessing requirements to a level such that ASIR techniques can be reasonably introduced into standard daily radiology practice without sacrifice in time or quality. This should lead to a substantial reduction in patient radiation doses, especially in those who undergo multiple CT scans, such as patients with recurrent urolithiasis. Additionally, these techniques should be applicable in patients undergoing multiphase CT-urograms for management of urinary tract malignancies, further emphasizing the potential for radiation dose reduction in patients with varying renal diseases.

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Diffusion Tensor Imaging of the Kidney

By Richard Beegle

Advances in magnetic resonance (MR) technology have not only improved anatomic detail but have also allowed for functional analysis of the kidney. Functional MR imaging is noninvasive and does not require intravenous gadolinium-based MR contrast agents, which can be harmful in patients with impaired renal function who are susceptible to nephrogenic systemic fibrosis. Functional MR techniques include diffusion weighted imaging (DWI) and diffusion tensor imaging (DTI).

DWI measures the motion of water in tissues due to inherent Brownian motion of water and can be quantified by the apparent diffusion coefficient (ADC). With DTI, the fractional anisotropy (FA) of tissues is assessed, which measures the directionality and degree of diffusion (1). Due to the anatomic structure of the kidney in a radial orientation, the motion of water molecules tends to be along the direction of the renal tubules. In addition, DTI may also be able to characterize the microstructural environment of the kidneys and reveal pathologic processes occurring within them.

Recent research has revealed multiple clinical applications for DTI in the evaluation of kidneys ranging from monitoring diabetic nephropathy to evaluating renal transplants and neoplasms. Lanzman et al. (2) have shown the utility of DTI in the evaluation of renal allografts. In kidneys with normal function, FA values are higher in the renal medulla than the renal cortex, likely owing to the radial arrangement of tubules, collecting ducts, and vessels. In renal allografts, which have poor renal function in the setting of acute tubular necrosis or acute rejection, the FA values are significantly lower and there is a loss of the corticomedullary differentiation.

Ischemic reperfusion injury is another cause of acute renal failure that has been identified in renal transplantation, shock, and vascular surgery (3). Ischemic reperfusion injury leads to changes in the microstructure of the kidney through microvascular and tubular injury, cell swelling, and impaired glomerular filtration rate and renal hemodynamics (3). These changes disrupt the radial microstructure of the kidney leading to disruption of the normal diffusion and decrease in the FA and ADC values.

DTI may also be valuable for detection and monitoring of diabetic nephropathy. Diabetes can cause changes in the microstructure of the kidney, for example glomerulosclerosis, interstitial fibrosis, and tubular damage. These changes to the microstructure may be the cause of the decrease in FA values within the kidney, especially within the renal medulla (4). The decrease in FA values within the renal medulla has been seen in diabetics with normal renal function. Therefore, MR imaging can possibly be used to detect early changes of diabetic nephropathy (5).

Functional MR imaging, especially DWI, is a noninvasive technique that is rapidly advancing and shows promise in providing renal pathophysiology without the need for intravenous contrast agents. While these methods have exciting potential, the actual clinical utility has yet to be determined.

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Recent Advances in Imaging of Renovascular Hypertension

By Abeer Ahmed

Renovascular disease is an uncommon but potentially treatable cause of secondary hypertension. It accounts for less than 1 percent of cases of mild to moderate hypertension (1), but with a higher frequency among those with severe or refractory hypertension (2). In the past, conventional angiography has been the gold standard diagnostic test for renal artery stenosis. Unfortunately, the test is expensive, invasive, exposes the patient to ionizing radiation, and requires nephrotoxic contrast material. Not all angiographically demonstrated vessel narrowing results in renal hypertension, and angiography does not allow for interpretation of the physiologic significance of the stenosis. Other noninvasive imaging tests are now recommended prior to conventional angiography, which include Doppler ultrasound, angiotensin converting enzyme (ACE)–inhibitor renal scintigraphy, computed tomography (CT) angiography (CTA), and magnetic resonance angiography (MRA).

Often the initial diagnostic test of choice is Doppler ultrasound because of its relative low cost and lack of ionizing radiation. Although it allows direct evaluation of the renal vasculature, Doppler ultrasound is usually an indirect method for evaluating the main renal artery since the proximal renal artery can be difficult to visualize owing to bowel gas. In addition, ultrasound is dependent on the skill of the operator, and patient-related issues—such as patient body build and size, as well as ability to cooperate—can compromise the study.

ACE inhibition renography can be an accurate screening tool for significant renal artery hypertension but it performs poorly in the setting of bilateral renal artery disease. Renography has fallen into disuse with the development of new hardware and software in CT and MRI.

CTA and MRA have risen to the forefront in renal artery evaluation. CTA can provide semiquantitative evaluation of renal artery stenosis and stent patency with a short image acquisition time. Disadvantages of this technique include the need for iodinated contrast and exposure to ionizing radiation. This is an anatomic visualization of the arteries and does not determine physiologic significance.

MRA, which includes time-of-flight (TOF) imaging and phase contrast, has become a substitute for CTA. TOF imaging and phase contrast uses pulse sequences to brighten blood within the vessel lumen. The disadvantages of traditional MRA are artifacts related to patient motion and breathing, limited image quality due to signal loss, and lack of ability to evaluate the entire course of the renal artery due to the oblique orientation of the artery in relation to the aorta.

Recent advances in MR technology software have allowed development of sequences such as time-resolved MRA and 2D projection MRA that provide information similar to that of conventional angiography. Time-resolved MRA, as opposed to traditional MRA, has a high spatial and temporal resolution that allows for detection of complex flow patterns, which is not possible with other techniques. In addition, 3D volume acquisition can also be obtained, which allows for greater anatomic coverage without sacrificing image quality and provides the ability to segment the renal artery for better analysis. 2D projection MRA has an advantage of being faster than 3D imaging and allows for a single, thicker slice, which can evaluate the entire course of the vessel accurately. In addition, 2D MR digital subtraction (DS) angiography can also be performed resulting in similar images to that of conventional x-ray DS angiography. The newer sequences allow robust MRA imaging even without the use of intravenous contrast. There are also new sequences that allow renal artery flow quantification adding physiologic information to the anatomic study.

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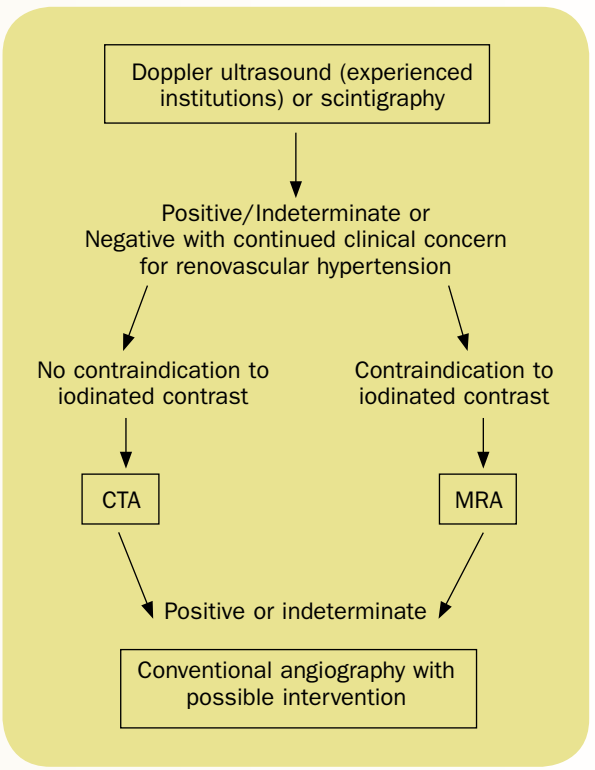
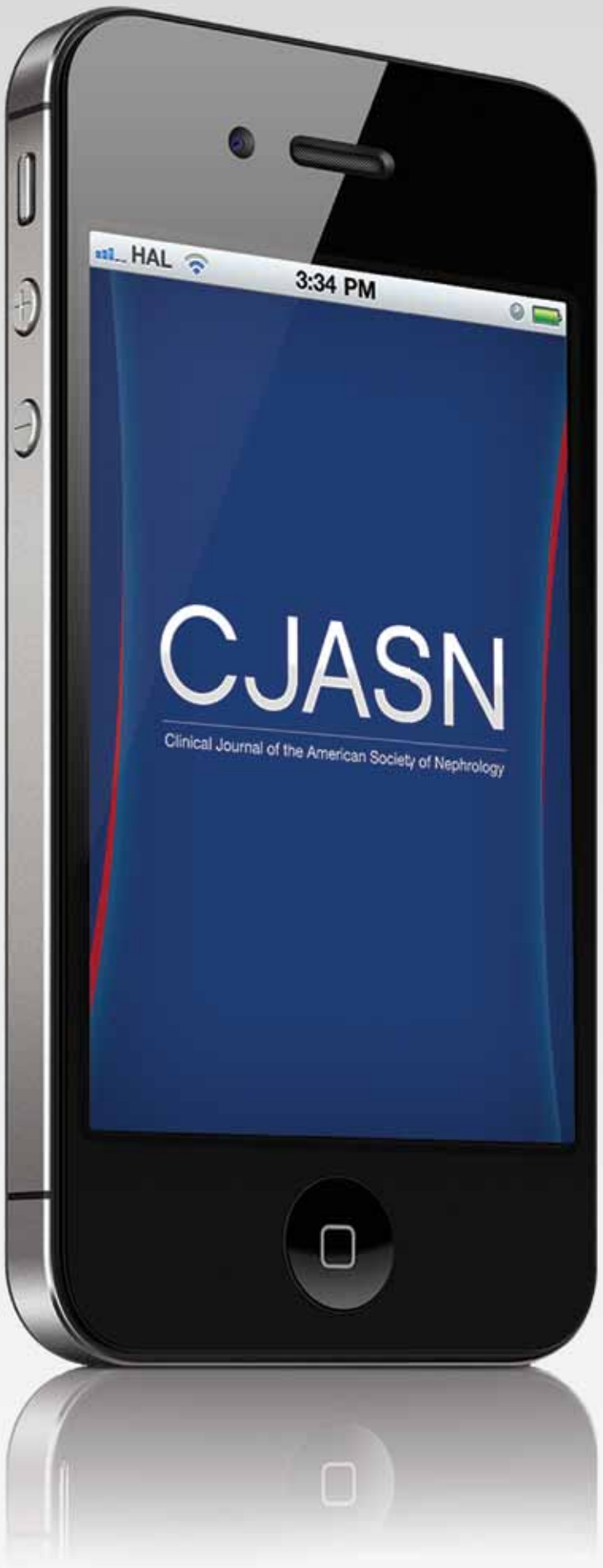


Abbreviations: CTA = computed tomography angiograpy; MRA = magnetic resonance angiography.



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ASN LEADING THE FIGHT AGAINST KIDNEY DISEASE

Journal View

A Urine Test for Acute Kidney Rejection?

A new test based on a "three-gene signature" can detect acute rejection of kidney allografts well before diagnosis by biopsy, according to a report in the *New England Journal of Medicine*.

In prospective, blinded fashion, the researchers developed the test using 4300 urine samples from 485 kidney allograft recipients, collected from 3 days through 12 months after transplantation. The goal was to identify messenger RNA (mRNA) levels in urinary cells that were correlated with the presence of acute graft rejection.

Normalized for 18S ribosomal RNA (rRNA) level, the combination of CD3ε mRNA, IFN-inducible protein 10 (IP-10) mRNA, and 18S rRNA provided a three-gene signature capable of differentiating between the presence and absence of rejection on allograft biopsy specimens. On receiver operating characteristic curve analysis, the area under the curve was 0.85 in the development set and 0.74 in an independent validation set.

The three-gene signature distinguished acute cellular rejection from acute antibody-mediated and borderline rejection. It also permitted diagnosis of acute cellular rejection in patients receiving anti–IL-2 antibodies versus T cell–depleting antibodies. Test performance was unaffected by the presence of urinary tract infection.

The average trajectory of the three-gene signature increased significantly in the weeks before the diagnosis of acute rejection could be made in biopsy specimens. By contrast, in patients without rejection, the level remained below the diagnostic threshold.

A molecular signature consisting of CD3ε mRNA, IP-10 mRNA, and 18S rRNA levels detected in urinary cells provides a promising, noninvasive test for acute rejection after kidney allograft transplantation. The three-gene signature "may provide a direct measure of risk…and a means of assessing immune status with repeated assessments," the investigators said. With further evaluation, the test could be useful in the earlier identification of acute rejection, permitting individualized immunosuppressive therapy [Suthanthiran M, et al. Urinary-cell mRNA profile and acute cellular rejection in kidney allografts. *N Engl J Med* 2013; 369:20–31].

Bile Casts Found in Kidney Injury with Severe Liver Dysfunction

Renal bile casts are common in patients with severe hepatic dysfunction, and they may play an important role in the development of kidney injury, reports a study in *Kidney International*.

The clinicopathologic study included 44 patients with confirmed jaundice, identified at one university pathology department between 2004 and 2011. The presence and associations of intrarenal bile cast formation were analyzed by use of autopsy specimens in 41 cases and renal biopsy specimens in three.

Bile casts involving distal nephron segments were found in 24 of the 44 jaundiced patients. Bile cast nephropathy was considered mild in 16 cases but severe in eight, with extension to the proximal tubules. Tubular bile casts were found in 11 of 13 patients with hepatorenal syndrome and in all 10 with alcoholic cirrhosis. Jaundiced patients with bile casts had significantly increased total and direct bilirubin levels, with a trend toward increased creatinine and liver enzyme levels.

Published studies from the 1950s and 1960s reported on intrarenal bile casts as a mechanism of kidney dysfunction in patients with liver failure—previously termed "cholemic nephrosis" or "bile nephrosis." However, in recent years lit-

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Journal View

Bile Casts

Continued from page 13

tle attention has been given to the concept of cholemic nephrosis or the pathologic relevance of renal bile casts.

The new study shows a high rate of intrarenal bile casts among patients with clinical jaundice. Bile casts may contribute to kidney injury via direct bile and bilirubin toxicity as well as by tubular obstruction.

The authors propose the term "bile cast nephropathy" as a condition causing impaired renal function in patients with severe liver dysfunction. It can affect adults and children with a wide range of hepatic disorders, with or without cirrhosis. The researchers call for further studies to clarify the prognostic and clinical implications of bile cast nephropathy [van Slambrouck CM, et al. Bile cast nephropathy is a common pathologic finding for kidney injury associated with severe liver dysfunction. *Kidney Int* 2013; 84:192–197].

Antimicrobials May Lower Risk of Urinary Tract Infection After Catheterization

For hospitalized patients with short-term urinary catheterization, giving antibiotics after catheter removal can reduce the risk of urinary tract infection (UTI), according to a meta-analysis in the *British Medical Journal*.

A systematic review of the literature identified seven controlled trials, six of them randomized, of antimicrobial treatment to prevent symptomatic UTI after removal of a short-term urinary catheter (14 days or less). The meta-analysis included data on 665 patients taking various antimicrobial drugs, for various durations, and 855 taking control treatments. Most of the studies included postoperative patients.

On pooled data analysis, there was a 5.8 percent absolute reduction in UTI risk in patients taking antimicrobial prophylaxis. The risk ratio for UTI in the antimicrobial group was 0.45. Seventeen patients had to be treated with antimicrobial prophylaxis to prevent one UTI.

Even with prompt catheter removal, hospitalized patients with urinary catheterization are at risk of UTI. Despite previous randomized trials, the benefits of antimicrobial prophylaxis in reducing this risk are unclear.

The new meta-analysis suggests a reduction of more than one-half of the risk of UTI for patients receiving antimicrobial prophylaxis after short-term catheterization. Further studies are needed to identify the patient subgroups most likely to benefit from antimicrobial prophylaxis, with attention to minimizing side effects, costs, and antimicrobial resistance [Marschall J, et al. Antibiotic prophylaxis for urinary tract infections after removal of urinary catheter: meta-analysis. *BMJ* 2013; 346:f3263].

BP Phone Home: Telemonitoring Helps Control BP

A home telemonitoring intervention, including case management by pharmacists, led to significant and lasting reductions in BP, reports the *Journal of the American Medical Association*.

The HyperLink trial included 450 adults with uncontrolled BP, enrolled at 16 primary care clinics in an integrated health care system in Minneapolis/St Paul. One group of practices received the home telemonitoring intervention, in which patients were instructed to perform at least six BP measurements per week (three in the morning, three in the evening). The study pharmacists acted as case managers, adjusting antihypertensive therapy in response to the home BP readings. The control practices followed usual care.

The intervention and control groups were compared for rates of target BP below 140/90 mm Hg, or 130/80 mm Hg in patients with diabetes or chronic kidney disease. Assessment included 6 months of follow-up after the 12-month intervention period.

The mean age was 61 years, and 55 percent of patients were men. At baseline, the mean BP was 148/85 mm Hg, and patients were taking a mean of 1.5 antihypertensive drugs.

Home telemonitoring was associated with a significant increase in the number of patients meeting the criteria for BP control: 57.2 versus 30.0 percent at both 6 and 12 months. Six months after the intervention period, the rates were 71.8 and 57.1 percent, respectively.

The telemonitoring group had greater reductions in systolic BP, with differences of 16.7 mm Hg at 6 months, 9.7 mm Hg at 12 months, and 6.6 mm Hg at 18 months. The differences in diastolic BP were 6.0, 5.1, and 6.3 mm Hg, respectively. Telemonitoring was also associated with more intensified antihypertensive therapy, increased adherence to medications and sodium restriction, and some improvements in patient satisfaction. Safety was acceptable, although some patients at the lower BP target had hypotension-related events.

The HyperLink intervention, incorporating home BP monitoring and team-based care, reduced BP in patients with uncontrolled hypertension, compared with usual care. The intervention costs are estimated at $1350 per patient per year. The authors plan further evaluations of cost-effectiveness and long-term cost savings [Margolis KL, et al. Effect of home blood pressure telemonitoring and pharmacist management on blood pressure control: A cluster randomized clinical trial. *JAMA* 2013; 310:46–56].

Policy Update

Proposed Cuts to ESRD Program Could Limit Access to Care

Kidney community rallies to respond

By Rachel Shaffer

A recent proposal from the Centers for Medicare and Medicaid Services (CMS) to reduce the End Stage Renal Disease (ESRD) program bundle by 12 percent has generated concern throughout the kidney community. The July 1 proposed rule recommends several other changes to the ESRD Prospective Payment System (PPS) and Quality Incentive Program (QIP) but the focus and concern from ASN—as well as other health professional organizations, patient groups, dialysis providers, and industry—remains the significant proposed payment reduction.

If implemented, cuts to the ESRD program of the magnitude CMS proposed could have negative consequences for patients and dialysis units in certain parts of the country—with certain populations disproportionality affected.

"More than 20 million Americans have kidney disease, and the Medicare ESRD program provides life-saving care to nearly 400,000 beneficiaries with kidney failure," said ASN President Bruce A. Molitoris, MD, FASN. "People with kidney disease, among the most vulnerable patients, are disproportionately underrepresented minorities, and such a large cut may reduce access to care and quality of treatment."

Should the proposed cut take effect, it would likely endanger the existence of some dialysis units—especially rural, inner-city, and smaller clinics—making it much more difficult for people who rely on those clinics for life-saving dialysis at least 3 times a week to access that therapy.

Each year during midsummer, CMS releases a proposed rule typically adjusting the base PPS rate to reflect changes in price (known as the market basket), modify the QIP, and make other adjustments to the ESRD program. Earlier this year, however, Congress directed CMS to re-examine the ESRD PPS base rate from the perspective of utilization (rather than price, as it does on an annual basis). Specifically, the American Taxpayer Relief Act of 2013 mandated that CMS compare use of drugs and biologics in 2007 to use of drugs and biologics in 2012, and adjust the payment rate accordingly.

That comparison yields a 12 percent cut to the ESRD program, according to CMS. Together with the annual market basket update, which this year would provide a 2.6 percent increase based on recent price changes, the total cut would amount to 9.4 percent.

To put this proposed cut in perspective, the Medicare Payment Advisory Commission's (MedPAC) March 2013 Report to the Congress projects a Medicare margin of just 3 percent to 4 percent for dialysis providers. While the exact methodology CMS used to calculate the base rate—and whether the agency is acting according to the statute—remains unknown or contested, the fact remains that a cut of the scale proposed could have a deleterious effect on patient access to high-quality care.

"It's troubling that Congress mandated a payment reduction at the same time that CMS is using the ESRD program as a model for bundled payment, a quality incentive program, and a specialty-specific integrated care delivery model," said Thomas H. Hostetter, MD, ASN Public Policy Board chair. "The kidney community is working diligently on achieving the goals of the Quality Incentive Program, which was also mandated by Congress and implemented by CMS, in order to avoid further cuts in reimbursement."

ASN, together with the broader kidney community, is taking action to ensure that CMS follows Congress' directive to re-examine the base rate payment in a manner that protects the vulnerable kidney patient population. In addition to highlighting the potential unintended consequences of CMS' proposed payment reduction in press releases and on social media, ASN is joining other organizations in asking Congress to weigh in to support patients with kidney disease. As of press time, at least 13 members of the U.S. House of Representatives had signed on to a letter to CMS Administrator Marilyn Tavenner urging CMS to carefully consider the impact of proposed cuts, pointing out that every congressional district has patients dependent on the ESRD Program. ASN will continue to help call congressional attention to the situation, and will submit comments to CMS regarding its proposals and recommending alternatives—as well as urging CMS to closely track the care patients on dialysis receive to guarantee that any payment reductions do not have unintended consequences.

"ASN, the rest of the kidney community, and CMS must work together to provide the highest quality care possible to the millions of Americans with kidney disease, including those on dialysis whose lives are saved daily by the Medicare ESRD Program," Molitoris said.

Visit ASN's website for more information and responses from the society on this important issue.

ASN Meets with CMS Administrator Tavenner, Other Top CMS Leaders

By Rachel Shaffer

Bringing ASN's perspectives on key issues and programs affecting patients with kidney disease, ASN President Bruce A. Molitoris, MD, FASN, and ASN Public Policy Board chair Thomas H. Hostetter met with top leaders at the Centers for Medicare and Medicaid Services (CMS) in June.

"Both ASN and CMS share the goal of delivering the best possible care to patients with chronic kidney disease (CKD) and end stage renal disease (ESRD)," Hostetter said. "This meeting was an opportunity to discuss recommendations ASN has for improving the good work CMS is already doing in various programs and to reiterate the society's strong desire to serve as an objective, evidence-based resource for the agency as possible."

Recently confirmed CMS Administrator Marilyn Tavenner participated in the discussion, joined by Director for Medicare and Deputy Administrator Jonathan Blum, Chief Medical Officer Patrick Conway, MD—who was also recently appointed as the Interim Director of the Centers for Medicare and Medicaid Innovation—Deputy Chief Medical Officer Shari Ling, MD, and Chief of Staff Aryana Khalid.

Blum will be speaking at ASN Kidney Week 2013 as the Christopher R. Blagg Endowed Lecturer.

The discussion covered a range of topics, including the potential rebasing of the ESRD bundle. The ASN leaders emphasized concern that rebasing the bundle not adversely impact ESRD patient care or quality outcomes, and that ASN wants to work with the agency to ensure monitoring of appropriate patient access and outcomes to maintain the quality of care the society has come to expect through the implementation of the bundle and Quality Incentive Program.

ASN reiterated that the ESRD bundled payment should cover the actual cost of providing services to beneficiaries, and that a rebased bundle must maintain the flexibility to preserve the physician-patient relationship and ensure that the most appropriate, personalized treatment is available to each individual. ASN continues to articulate concerns that CMS appropriately rebase the bundle in a manner that protects patient access to care (see article, above).

The Medicare Shared Savings Program was another focus of the conversation, particularly ASN's recommendations for improving the ESRD Seamless Care Organization (ESCO) Program. ASN placed special emphasis on the importance of strategies to promote transplantation in ESCOs. For most patients, kidney transplantation is the optimal form of renal replacement therapy; ASN concurred with CMS that that increased transplantation rates are essential to achieving the Comprehensive ESRD Care Initiative's goals. However, transplant candidates tend to be the healthiest patients and, by extension, the least costly and complicated dialysis patients. Given that patients who receive a kidney transplant are no longer attributed to an ESCO, ASN expressed concerned that there is an unintended incentive to not transplant patients who would be good candidates for care through ESCOs, and offered to collaborate with CMS to develop a solution to prevent this potential unintended consequence.

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Policy Update

Tavenner

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Table 1 summarizes the recommendations ASN made to CMS regarding the ESCO program.

Tavenner and Blum were also interested in ASN's recommendations regarding how to improve the care of patients with CKD in "general" Accountable Care Organizations, both in terms of quality measures and care delivery concepts. CMS leadership recognized that some of the greatest opportunities for savings in kidney care occur in the late stages of CKD—such as vascular access placement and consideration of home dialysis—and ASN anticipates further exchange with the agency on this issue in the future.

"I believe that this opportunity for dialogue and exchange of ideas with Ms. Tavenner and her colleagues at the highest levels of CMS leadership helped to solidify ASN as a thoughtful resource on all issues related to kidney care for the agency," Hostetter said. "It is my hope that ASN can continue to build this relationship, with the ultimate goal of helping CMS continually improve the quality of care our patients receive."

Table 1. Top ASN Recommendations for the ESCO Program

1.	Develop dialysis-specific quality metrics in a transparent manner that allows for community input.
2.	Prospectively specify the criteria that determine whether an ESCO is deemed "successful" or "unsuccessful."
3.	Develop a plan to ensure consistent access to transplantation, recognizing that the best candidates for transplant are also often likely to be the healthiest patients on dialysis, and will not be attributed to the ESCO posttransplant.
4.	Facilitate research into and better understanding of optimal dialysis care by sharing de-identified ESCO patient data with qualified investigators, similar to the National Institutes of Health.
5.	Preferentially match patients on dialysis to ESCOs over other types of Medicare Shared Savings Programs (MSSP), reflecting the fact that ESCOs are specifically designed to improve care for this vulnerable patient population.
6.	Establish and explain safeguards to monitor and address "cherry picking" or potential changes in patient outcomes.
7.	Allow nephrologists to both participate as specialists in an ACO and own an ESCO in the same market.
8.	Continue to emphasize the leadership role of the nephrologist in nephrology practice.
9.	Permit reasonable use of waivers as a tool to improve patient care.
10.	Reconsider the goal of rebasing the program in years four and five, recognizing that this approach penalizes the highest performing ESCOs.

The (Un)Sustainable Growth Rate

By Mark Lukaszewski

It's not every day that the House, Senate, and Congressional Budget Office (CBO) agree on something, but all three concur that the sustainable growth rate (SGR) has to go. In an attempt to control Medicare spending on physicians' fees, Congress enacted the SGR formula in 1997. Although it has called for dramatic reductions in payments over the past decade, each year Congress has temporarily overridden the cuts and kept the SGR in place. According to the formula, physician fees should have been reduced by 27 percent on January 1, 2013, which could have a devastating effect on Medicare and the patients who rely on it. Now, for the first time since its conception, Congress is starting to admit there is a problem with the SGR, and both parties have recognized that the time to act is now.

Keeping score

To understand why legislators are so focused on the SGR and so motivated to work in bipartisan unity, you first have to understand the CBO and its all-important scoring process. For every bill that costs money to implement, the CBO issues a report estimating its cost over a 10-year period based on economic projections and other factors. This cost estimate is the bill's "score." If new data become available, the CBO can rescore a bill before the end of its 10-year period, which can be a critical factor. In February 2013, the CBO released a new report stating the cost of repealing the SGR system had been overestimated by nearly a billion dollars. It became apparent that it would cost more to fix the SGR than it would to abandon it and start from scratch.

The House made the first public move toward eliminating the SGR in February, with Rep. Joe Heck (R-NV) and Rep. Alyson Schwartz (D-PA) introducing the Medicare Physician Payment Innovation Act of 2013 (H.R. 574). Besides eliminating SGR, this bill seeks to institute annual reviews of physician payments, implement comprehensive preventive and primary care services, secure uniform payment rates, and stabilize the Medicare physician payment system as a whole.

The leadership of the House Energy and Commerce Committee (which oversees health) also drafted a bipartisan "prelegislation"—a discussion draft designed to promote conversation. This prelegislation proposes to repeal SGR by improving the fee-for-service program, eventually phasing in predictable alternate payment models. It would institute a three-phase process, with advancement predicated on the success of the previous phase. Each phase would afford physicians the opportunity to "opt-out" of the modified fee-for-service payment system and allow them to join an alternate payment model system.

This prelegislation also calls for a transition period for physicians during which current payment incentives—such as the Physician Quality Reporting Program (PQRS) and Electronic Health Record Meaningful Use Program—would still be applicable for a 5-year period. The legislation also proposes an annual payment increase of 0.5 percent per year. After the transition period, reimbursement would be tied to performance on quality measures.

Although the prelegislation has substantial bipartisan support and appears to improve payment accuracy for providers, it has not yet been given an official name or resolution number—two necessary legislative steps for it to reach the House floor for consideration.

The Senate is also feeling the pressure to replace the SGR. In May, Senate Finance Committee Chairman Max Baucus (D-MT) and ranking Member Orrin Hatch (R-UT) released a joint statement to the health care provider community outlining goals similar to the House initiatives. Both senators agree that repealing SGR is a top priority for their committee. The Senate has offered fewer specifics about what a replacement plan would look like, but has generally stated that physician services be appropriately valued, and that incentive payments for physicians would likely facilitate reduced Medicare spending growth.

As of press time, it is uncertain whether the House bill will gain support, or if the Senate will draft a bill of its own. While the exact solution has yet to take shape, Congress' interest in replacing SGR remains greater than it has been in at least a decade—a promising sign. ASN strongly supports efforts to replace the SGR with a more stable system that accurately reflects the value of physicians' care, and is closely monitoring this issue on Capitol Hill. Stay tuned to *ASN Kidney News* as well as email communications from ASN to learn how you can get involved in advocating for a replacement to SGR.

ASN Goes to NIH and the VA

By Grant Olan

ASN President Bruce A. Molitoris, MD, FASN, President-Elect Sharon M. Moe, MD, FASN, Councilor Raymond C. Harris, MD, FASN, and Research Advocacy Committee members in June visited with National Institutes of Health (NIH) leaders and staff for "Kidney Research Advocacy Day."

NIH's 27 institutes and centers are engaged in global health research and research training activities. For the second straight year, ASN met with senior staff at the National Institute of Diabetes and Digestive and Kidney Diseases, National Institute on Aging, National Institute of Minority Health and Health Disparities, and Center for Scientific Review. ASN also had a first-ever meeting with senior staff at the Department of Veterans Affairs (VA) Office of Research and Development.

Recurring concerns discussed in the meetings included 1) available grant funding opportunities that have not been optimally pursued by kidney community investigators, 2) the importance of collaboration among NIH institutes and other federal agencies on kidney-related studies and research training, 3) the importance of including patients with kidney disease in kidney-related clinical trials, and 4) the need to step up advocacy to protect NIH from continued budget cuts.

Since the doubling of NIH's budget ended in 2002, NIH's budget has essentially been undoubled after adjusting for biomedical research inflation. As a result, research budgets have been slashed, programs have been axed, and grant application success rates have fallen from 31.2% in 2002 to nearly 17% in 2012.

This past April, patient advocates from the American Association of Kidney Patients (AAKP) and Dialysis Patient Citizens (DPC) joined ASN leaders for meetings with nearly 60 congressional offices in the House and Senate to advocate for the society's top policy priorities, including more funding for kidney research.

Here are some takeaways from each of the Kidney Research Advocacy Day meetings.

National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)

Dr. Molitoris, Dr. Moe, and Research Advocacy Committee members met with NIDDK Director Griffin P. Rodgers, MD; Kidney, Urologic, and Hematologic Diseases Division Director Robert A. Star, MD; and other senior staff. In addition to the concerns mentioned earlier, ASN and NIDDK discussed better communication with the public about institute initiatives, plans, and research opportunities, and additional opportunities for NIDDK involvement and participation at Kidney Week.

National Institute on Aging (NIA)

Research Advocacy Committee members met with NIA Director Richard J. Hodes, MD, Deputy Director Marie A. Bernard, MD, and other senior staff. ASN and NIA discussed future and current studies related to the deleterious effects of kidney disease on aging, and additional opportunities for NIA involvement and participation in ASN activities.

National Institute of Minority Health and Health Disparities (NIMHD)

Dr. Molitoris, Dr. Moe, and Research Advocacy Committee members met with NIMHD Office of Extramural Research Administration Director Francisco S. Sy, MD, DrPH, and Irene Dankwa-Mullan, MD, in the Division of Scientific Programs. As part of NIMHD's mission, the institute "plans, reviews, coordinates, and evaluates all minority health and health disparities research and activities of the National Institutes of Health." NIMHD is aware of the enormous racial and ethnic disparities in kidney disease and described institute programs available to help minority kidney scientists with professional development and research. More information is available at http://www.nimhd.nih.gov/.

Center for Scientific Review (CSR)

Dr. Molitoris; Dr. Moe; and Research Advocacy Committee members met with Donald Schneider, PhD, Senior Advisor to the Director of CSR; Division of Physiological and Pathological Sciences Director Seymour Garte, PhD; and other senior staff members. Topics discussed included the decreasing number of R01 investigator-intiated grant applications, ensuring the participation of kidney experts on study sections, the review of kidney-related applications by the best sections, and a possible CSR informational session on the grant application review process at Kidney Week.

VA Office of Research and Development (ORD)

Dr. Harris and Research Advocacy Committee members met with ORD Biomedical Laboratory Research & Development Acting Director Ronald Pzrygodski, MD, and a number of other senior staff members. ORD noted that more than 200,000 veterans have kidney disease and that a preponderance of that population has type 2 diabetes. ORD described a number of current studies that patients with kidney disease stand to benefit from, including the Million Veterans Program to study how genes affect health. ORD is interested in continued collaboration with ASN.

Table 1 lists ASN Research Advocacy Committee members.

Please check back for information in the next *Kidney News* about new federal grant funding opportunities for kidney investigators.

NIDDK Director Dr. Rodgers greets Dr. Leonard from ASN as the meeting begins.

ASN President-Elect Dr. Moe inquires how CSR assigns grant applications to study sections.

NIDDK's Dr. Star (second from left) poses for a picture with (left to right) Dr. Feldman, Dr. Molitoris, and Dr. Sedor from ASN.

ASN's Dr. Sharma (back right) addresses concerns about the decreasing number of R01 investigator-intiated grant applications.

How have NIH budget cuts affected your research?

ASN recently launched a survey to collect member feedback on how cuts might affect (or have affected) them to share with Congress. The society is also seeking volunteers to provide members of Congress and their staff with tours of their labs or institutions to foster support for medical research. To complete the survey and volunteer, go to http://www.surveymonkey.com/s/XYBFX6Q.

Table 1. Research Advocacy Committee members

- L. Ebony Boulware, MD
- Frank C. Brosius, III, MD
- Josef Coresh, MD, PhD, FASN
- Harold I. Feldman, MD, FASN
- Linda F. Fried, MD, FASN
- T. Alp Ikizler, MD, FASN
- Jordan A. Kreidberg, MD, PhD
- Mary B. Leonard, MD
- Kumar Sharma, MD
- Michelle P. Winn, MD
- John R. Sedor, MD, Chair

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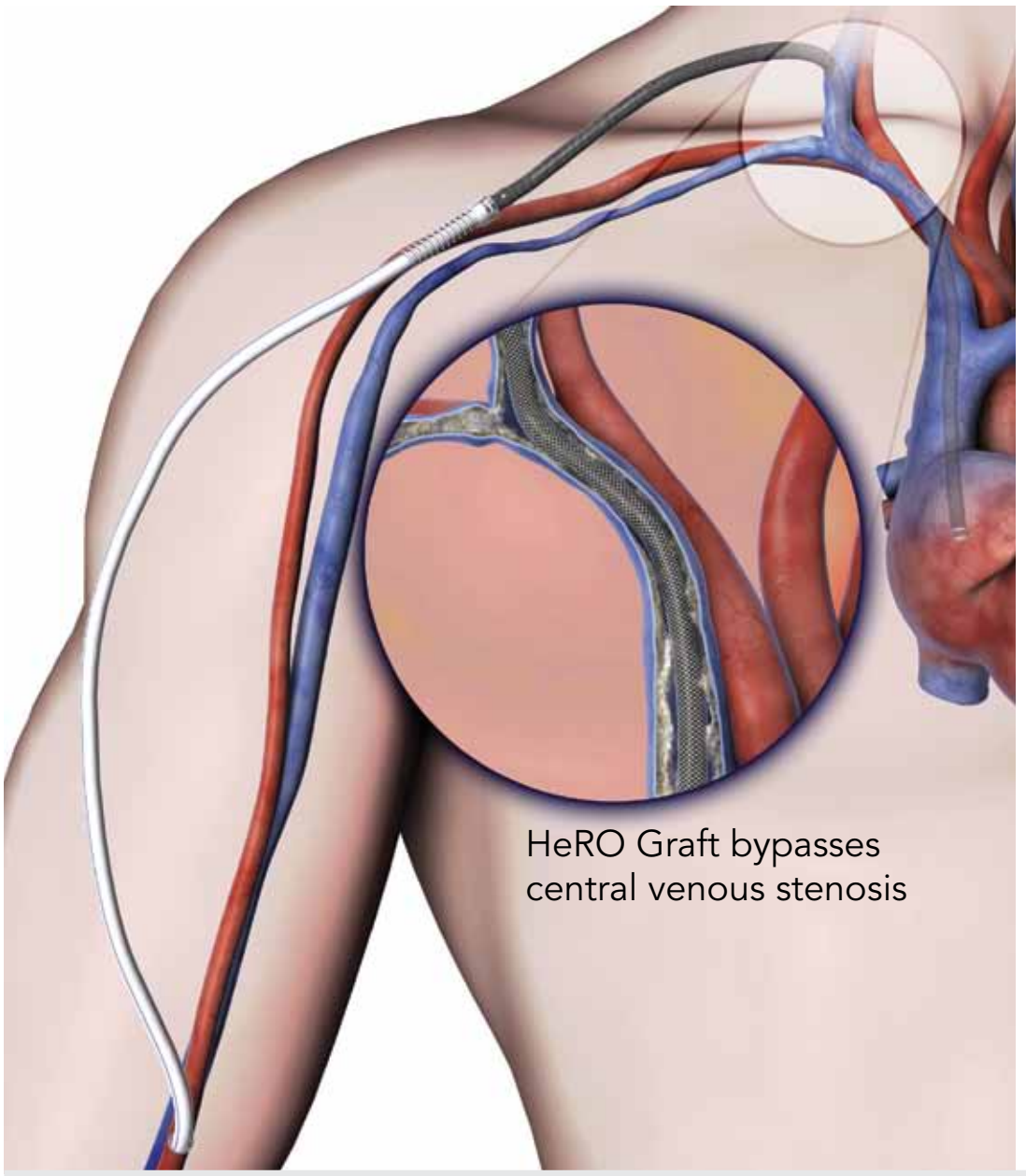

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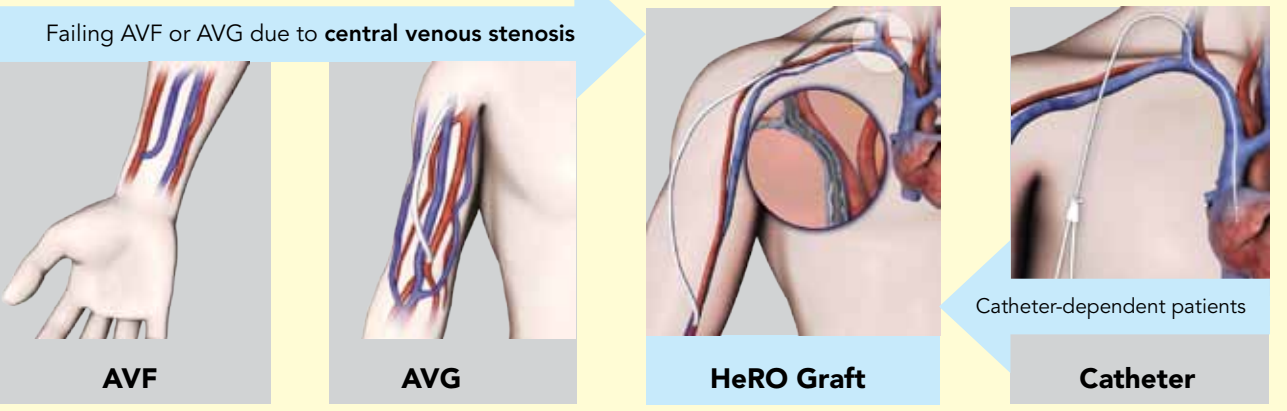

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References:
1) Katzman et al., J Vasc Surg 2009. 2) Gage et al., EJVES 2012. 3) Dageforde et al., JSR 2012.

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