Changes in Cognitive Function among Patients Undergoing Peritoneal Dialysis

Patients undergoing peritoneal dialysis as home-care therapy are required to self-monitor and self-manage their treatment; effective cognitive functioning is key for this patient population. However, the prevalence of cognitive impairment is high among patients with end-stage renal disease, with estimates of cognitive impairment ranging from 27% to 67%.

Previous studies have shown an association between cognitive impairment and mortality and technique failure. Results of an earlier multicenter cross-sectional survey conducted by Yu-hui Zhang, MD, and colleagues among peritoneal dialysis patients found a prevalence of cognitive impairment of 28.4%, assessed using the Modified Mini-Mental State Examination.

Dr. Zhang et al. recently conducted a multicenter prospective cohort study in five provinces in China to examine the risk factors for cognitive impairment in patients undergoing peritoneal dialysis as home care. The study was designed to assess change in cognitive function and the factors associated with the change among peritoneal dialysis patients by measuring cognitive function at baseline and then again after 2 years. Secondary end points were the effects of baseline cognitive impairment on all-cause and cardiovascular mortality, hospitalization, and transition to hemodialysis therapy. Study results were...
INDICATION
Velphoro® (sucroferric oxyhydroxide) is a phosphate binder indicated for the control of serum phosphorus levels in patients with chronic kidney disease on dialysis.

IMPORTANT SAFETY INFORMATION
- Velphoro chewable tablets must be administered with meals. Velphoro should be chewed or crushed. Do not swallow whole.
- Patients with peritonitis during peritoneal dialysis, significant gastric or hepatic disorders, following major gastrointestinal (GI) surgery, or with a history of hemochromatosis or other diseases with iron accumulation have not been included in clinical studies with Velphoro. Monitor effect and iron homeostasis in such patients.
- In a parallel design, fixed-dose study of 6 weeks duration, the most common adverse drug reactions to Velphoro chewable tablets in hemodialysis patients included discolored feces (12%) and diarrhea (8%).
- Velphoro can be administered concomitantly with oral calcitriol, ciprofloxacin, digoxin, enalapril, furosemide, HMG-CoA reductase inhibitors, hydrochlorothiazide, losartan, metoprolol, nifedipine, omeprazole, quinidine and warfarin. For oral medications where a reduction of bioavailability would be clinically significant consider separating of the timing of administration. Consider monitoring clinical responses or blood levels of the concomitant medications.

Please see Brief Summary on adjacent page or visit www.Velphoro.com for full Prescribing Information.

Updated KDIGO guidelines recommend limiting the use of calcium-based binders...

SWITCHING TO VELPHORO CAN MAKE A WORLD OF DIFFERENCE

Double the percentage of patients achieved phosphorus goal with half the pill burden*1

Visit RealWorldVelphoro.com TO SEE THE DIFFERENCE A SWITCH CAN MAKE

* A retrospective analysis of pharmacy data assessed the real-world effectiveness of Velphoro in 1,029 adult in-center hemodialysis patients who were switched to Velphoro during routine care. The study compared the proportion of patients with phosphorus levels ≤5.5 mg/dL, and the mean prescribed phosphate binder pills/day at baseline (3 months prior to Velphoro; binders included sevelamer carbonate, calcium acetate, and lanthanum carbonate) and during Velphoro follow-up (6 months after switch to Velphoro, n=424). This was a noninterventional analysis and did not impact prescriptions or prescribing patterns.1


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KDIGO = Kidney Disease: Improving Global Outcomes.
INDICATIONS AND USAGE
Velphoro (sucroferric oxyhydroxide) is a phosphate binder indicated for the control of serum phosphorus levels in patients with chronic kidney disease on dialysis.

DOSE AND ADMINISTRATION
Velphoro tablets must be chewed and not swallowed whole. To aid with chewing and swallowing, tablets may be crushed.

The recommended starting dose of Velphoro is 3 tablets (1,500 mg) per day, administered as 1 tablet (500 mg) 3 times daily with meals. Adjust by 1 tablet per day as needed until an acceptable serum phosphorus level is reached, with regular monitoring afterwards. Titrate as often as weekly.

DOSE FORMS AND STRENGTHS
Velphoro (sucroferric oxyhydroxide) chewable tablet 500 mg.

CONTRAINDICATIONS
None.

WARNINGS AND PRECAUTIONS
Patients with peritonitis during peritoneal dialysis, significant gastric or hepatic disorders, following major gastrointestinal surgery, or with a history of hemochromatosis or other diseases with iron accumulation have not been included in clinical studies with Velphoro. Monitor effect and iron homeostasis in such patients.

ADVERSE REACTIONS
In a parallel design, fixed-dose study of 6 weeks duration, the most common adverse drug reactions to Velphoro chewable tablets in hemodialysis patients included discolored feces (12%) and diarrhea (6%).

The following adverse reactions were identified during post-approval use of Velphoro and were reported voluntarily from a population of uncertain size.

Gastrointestinal Disorders: tooth discoloration
Skin and Subcutaneous Tissue Disorder: rash

To report SUSPECTED ADVERSE REACTIONS, contact Fresenius Medical Care North America at 1-800-323-5188 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS
Velphoro can be administered concomitantly with oral calcitriol, ciprofloxacin, digoxin, enalapril, furosemide, HMG-CoA reductase inhibitors, hydrochlorothiazide, losartan, metoprolol, nifedipine, omeprazole, quinidine and warfarin. Velphoro can be administered concomitantly with oral calcitriol, ciprofloxacin, digoxin, enalapril, furosemide, HMG-CoA reductase inhibitors, hydrochlorothiazide, losartan, metoprolol, nifedipine, omeprazole, quinidine and warfarin.

Inform patients to report any rash to their healthcare professional.

Inform patients that Velphoro can stain teeth.

Inform patients that Velphoro can cause discolored (black) stool, but this discoloration of the stool is considered normal with oral medications containing iron.

Inform patients that Velphoro tablets should be chewed or crushed. Do not swallow whole [see Dosage and Administration].

PATIENT COUNSELING INFORMATION
Inform patients that Velphoro should be chewed or crushed. Do not swallow whole [see Dosage and Administration]. Velphoro should be taken with meals. Instruct patients on concomitant medications that should be dosed apart from Velphoro [see Drug Interactions].

Inform patients that Velphoro can cause discolored (black) stool, but this discoloration of the stool is considered normal with oral medications containing iron.

Inform patients that Velphoro can stain teeth.

Inform patients to report any rash to their healthcare professional.

HOW SUPPLIED/STORAGE AND HANDLING

Velphoro are chewable tablets supplied as brown, circular, bi-planar tablets, embossed with “PA 500” on 1 side. Each tablet of Velphoro contains 500 mg iron as sucroferric oxyhydroxide. Velphoro tablets are packaged as follows:

NDC 49230-645-51 Bottle of 90 chewable tablets

Storage
Keep the bottle tightly closed in order to protect from moisture. Store at 25°C (77°F) with excursions permitted to 15 to 30°C (59 to 86°F).

PATIENT COUNSELING INFORMATION
Inform patients that Velphoro tablets should be chewed or crushed. Do not swallow whole [see Dosage and Administration]. Velphoro should be taken with meals. Instruct patients on concomitant medications that should be dosed apart from Velphoro [see Drug Interactions].

Inform patients that Velphoro can cause discolored (black) stool, but this discoloration of the stool is considered normal with oral medications containing iron.

Inform patients that Velphoro can stain teeth.

Inform patients to report any rash to their healthcare professional.

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Recent data on happiness among nephrologists should be a reason to celebrate the New Year. In the 2019 Medscape Physician Lifestyle and Happiness Report1 for “happiness outside work,” 58% of nephrologists are happiest outside work (the best ratings were for rheumatologists at 65% and the worst was for neurologists at 45%). If that were not enough, 65% of nephrologists had high self-esteem (only exceeded by plastic surgeons, urologists, ophthalmologists, endocrinologists, and orthopedists; the worst self-esteem was among infectious disease specialists at 47%).

Remarkably, 60% of nephrologists have happy marriages—only otolaryngologists, plastic surgeons, and urologists had happier marriages than nephrologists; psychiatrists had the least happy marriages.

The survey was of 15,069 physicians in 29 specialties, practicing medicine in the US, and weighted to the American Medical Association’s distribution by specialty and state. It was conducted between July and October 2018. About 45% of the respondents were over the age of 50 and 62% were male physicians.

One could legitimately quibble with the Medscape survey, arguing that it isn’t truly representative because of the relatively small number of nephrologists who were interviewed (approximately 150). Still, the findings were provocative because there seems to be a gap between how nephrologists regard themselves during their career versus the perceptions of nephrology as a subspecialty among fellows considering it as a career.

Recall that a paper by Jhaveri and colleagues in 2013 of 714 US internal medicine subspecialty fellows pointed to nephrology being an unpopular career choice2. According to the authors, “Most non-nephrology internal medicine subspecialty fellows never considered nephrology as a career choice. A significant proportion were dissuaded by factors such as the challenges of the patient population, lack of role models, lack of procedures, and perceived difficulty of the subject matter.”

Likewise a recent paper by Beckwith and colleagues from the UK reinforced the unpopularity of nephrology as a career3. The Beckwith study was based on semi-structured face-to-face interviews of 11 nephrologists followed by interpretative phenomenological analysis. One of the key findings was the importance of ‘inspirational’ role models.

Nephrology continues to grow as a specialty because the burden of kidney disease is rising steeply. According to Bowe and colleagues, in the United States alone from 2002 to 2016, the number of healthy life-years lost from chronic kidney disease increased 52.6%, to nearly 2 million. The complexity of our patients is well established. Yet, if we believe the survey data from US internal medicine fellows, nephrology isn’t thought much of as a career choice. Counter that with nephrologists, according to the Medscape survey, being in the top tier among subspecialists in happiness and esteem. Now there’s a happy message to begin the New Year!

REFERENCES
Mortality Rates in Medicaid Expansion States
continued from page 1

The primary outcome was 1-year mortality; secondary outcomes included insurance status, predialysis nephrology care, and type of vascular access for hemodialysis at the time of initiation of therapy.

The study population included 236,246 patients; of those, 142,724 were in expansion states and 93,522 were in nonexpansion states. Among those in the expansion states, mean age was 50.2 years, 40.2% were women, 40.2% were Hispanic. Among participants in the nonexpansion state group, mean age was 49.7 years, 42.4% were women, 40.2% were black, and 21.0% were Hispanic. Among participants in the nonexpansion state group, mean age was 49.7 years, 42.4% were women, 40.2% were black, and 17.8% were Hispanic.

The expansion state group was more likely to have diabetes and less likely to have hyper-tension as the primary cause of ESRD. The income eligibility levels for Medicaid were higher in 2013 and the rates of uninsurance for individuals 19 to 54 years of age were lower in expansion states compared with nonexpansion states. The mortality analyses were restricted to 180,044 patients who initiated dialysis prior to January 1, 2016, to identify deaths that occurred for up to 15 months following dialysis initiation.

Prior to 2014, mortality rates in expansion and nonexpansion states were similar; beginning in the first 6 months of 2014, mortality rates declined. In Medicaid expansion states, 1-year mortality following initiation of dialysis declined from 6.9% in the pre-expansion period to 6.1% following expansion (change, -0.8 percentage points; 95% confidence interval [CI], -1.1 to -0.5). In nonexpansion states, the mortality rates declined from 7.0% before expansion to 6.8% following expansion (change, -0.2 percentage points, 95% CI, -0.5 to 0.2), resulting in an adjusted absolute reduction in mortality in expansion states of 0.6 percentage points (95% CI, -1.0 to -0.2) and a relative mortality reduction of 8.5%. The difference-in-differences estimates were similar with and without multivariable adjustment.

In analyses by subgroup, adults 19 to 44 years of age experienced larger reductions in 1-year mortality (−1.1 percentage points; 95% CI, −2.1 to −0.3) compared with adults 45 to 64 years of age (−0.5 percentage points; 95% CI, −0.9 to −0.1; P = .01 for interaction). Among black patients, declines in 1-year mortality rates were larger compared with white patients (−1.4 percentage points; 95% CI, −2.2 to −0.7 vs −0.5 percentage points; 95% CI, −1.2 to 0.2; P = .04 for interaction). There were no statistically significant differences in adjusted mortality changes between Hispanic and white patients or for patients living in areas with poverty rates above versus below the median area-level poverty rate.

For the secondary end points, rates of Medicaid coverage for expansion and nonexpansion states diverged beginning in the first 6 months of 2014 when Medicaid coverage increased sharply in expansion states. There was a decline in the percentage of patients who were uninsured in both expansion and nonexpansion states; the decline was greater in the expansion states.

In expansion states, rates of initiating dialysis with an arteriovenous fistula or graft present were stable, but declined after 2014 in nonexpansion states. Following adjustment, there was an association between Medicaid expansion and a 10.5-percentage point increase in Medicaid coverage and a −4.2 percentage point decrease in being uninsured at the time of dialysis initiation (95% CI, 7.7–13.2 and −6.0 to −2.3, respectively) relative to nonexpansion states. There was a concurrent 1.0-percentage point increase in the proportion of patients receiving care from a nephrologist prior to initiation of dialysis and a 2.3-percentage point increase in initiating dialysis with a graft or fistula present (95% CI, −0.1 to 2.1 and 0.6–4.1, respectively).

Limitations to the study cited by the authors included the possibility that the findings may not be generalizable to patients with other chronic health care conditions, limiting the outcomes to two measures of nephrology care and 1-year mortality, and the lack of individual-level data on Medicaid eligibility. “Among patients with ESRD initiating dialysis, living in a state that expanded Medicaid under the ACA was associated with lower 1-year mortality. If this association is causal, further research is needed to understand what factors may have contributed to this finding,” the researchers said.
TAKEAWAY POINTS

Researchers in China conducted a multicenter, prospective cohort study to examine changes in cognitive function among patients receiving peritoneal dialysis as home-care therapy. Cognitive function was measured at baseline and after 2 years.

Among the 293 patients in the final analysis, the prevalence of cognitive impairments increased from 70.3% to 73.9% during the 2-year study period; however, executive function, immediate memory, and visuospatial skill improved over time.

Advanced age, lower education level, and depression were associated with deteriorated general and specific cognitive function.

Changes in Cognitive Function continued from page 1


Baseline data were collected from all participants for demographic characteristics, comorbid conditions, and biochemistry indexes. Assessments of cognitive function, depression, and sleep disorders were also made. Participants were followed-up prospectively. Patients who remained on peritoneal therapy between March 2015 and November 2015 underwent repeated measurements of biochemical indexes, cognitive function, depression, and sleep quality.

A total of 667 patients met eligibility requirements; of those, 493 provided participation consent. Baseline and follow-up cognitive testing measurements were available for 458 participants. Participants’ baseline data was comparable to general characteristics of the peritoneal dialysis population in China. Mean age was 51.6 years, peritoneal dialysis therapy duration was 25.1 months, body mass index was 22.9 kg/m², hemoglobin level was 10.4 g/L, and serum albumin level was 42.7 g/L. Of the 458 participants, 53.1% were men, 23.6% had diabetes mellitus, 21.0% had a history of cardiovascular disease, and 52.4% had a high school diploma or higher level of education.

During follow-up, 165 patients were excluded for various reasons. Reassessment of cognitive function was conducted for the remaining 293 patients. There were no differences in general or specific cognitive parameters between the excluded patients and the remaining patients; diabetes mellitus and serum high-sensitivity C-reactive protein (hs-CRP) were significantly higher in the excluded group compared with the remaining group (P=.006 and P=.004, respectively).

There were no other significant differences in demographic or biochemical data between the two groups.

At baseline, 19.7% (n=90) of participants were diagnosed with cognitive impairment; the 90 participants had significantly lower scores on tests of all specific cognitive functions compared with those with normal cognitive function. Compared with the normal cognitive function group, those in the cognitive impairment group were older, less educated, more likely to be female, and more likely to have diabetes mellitus, cardiovascular disease, and higher depression scores. They also tended to have lower serum albumin and calcium levels and higher hs-CRP and total cholesterol levels.

The prevalence of cognitive impairment increased from 19.8% (58/293) to 23.9% (70/293) during follow-up. At the same time, there was significant decrease in Modified Mini-Mental State Examination scores from 94.8 to 83.1 (P=.006). At the 2-year follow-up, the researchers observed better performance on the Trail-A and Trail-B tests that measure processing speed and executive function, and on immediate memory and visuospatial skill tests. There were no significant differences in scores for delayed memory and language ability between baseline and the 2-year follow-up.

There was significant association between advanced age, depression, and lower education level and worsening general cognitive function, and with several measures of specific cognitive function. Advanced age and lower education level were associated with poorer executive function and immediate memory, and depression was associated with impaired memory capacity and language ability.

At the 2-year follow-up, executive function performance tended to be worse among patients with diabetes mellitus. There was significant association between hyperglycemia and poorer general cognitive function, delayed memory capacity, visuospatial skills, and language ability. Higher levels of serum sodium contributed to the deterioration in delayed memory capacity and visuospatial skill.

There was no difference in mortality rates between patients with and without cognitive impairment. In univariable analysis, patients with executive dysfunction had an increased risk for all-cause mortality; the increase in risk disappeared following multivariable adjustments. Both global and specific cognitive impairment at baseline were associated with a greater rate of hospitalization. There was an association between memory dysfunction and a lower dialysis modality survival rate.

There were some limitations to the study cited by the researchers, including the relatively small number of deaths, the relatively short observation period, and potential selection bias due to the patients unavailable for the second assessment.

In summary, the researchers said, “The prevalence of cognitive impairment in our study increased over 2 years, although some specific cognitive function improved. In light of the inconsistencies among changes in various cognitive domains noted in our study, future studies exploring changes in both global and specific domains of cognitive function in other ethnic cohorts are warranted. Apart from the well-recognized risk factors for cognitive decline, hyperalbunineemia and depression were also significant risk factors for cognitive decline among peritoneal dialysis patients. Whether correcting these modifiable risk factors would slow down the decline in cognitive function warrants further investigation.”

Kidney Week.

TRC101 to Treat Patients with Chronic Kidney Disease and Metabolic Acidosis

San Diego—The risk of chronic kidney disease (CKD) progression is increased in patients with metabolic acidosis, and metabolic acidosis adversely affects muscle and bone. TRC101, a non-absorbed, sodium-free polymeric drug that selectively binds and removes hydrochloric acid from the gastrointestinal tract, is being developed to treat metabolic acidosis and slow the progression of CKD.

Donald E. Wesson, MD, MBA, of the Baylor Scott and White Health and Wellness Center, Dallas, Texas, reported results of a phase 3, double-blind, placebo-controlled trial of TRC101 in patients with CKD and metabolic acidosis in a late-breaking poster session at Kidney Week 2018. The poster was titled A Phase 3, Multicenter, Randomized, Double-Blind, Placebo-Controlled Trial to Treat Metabolic Acidosis in CKD Patients with TRC101, a Novel, Non-Absorbed Hydrochloric Acid Binder.

A total of 217 patients with CKD with metabolic acidosis were randomized in a 4:3 ratio to receive 6g TRC101 or placebo once-daily for 2 weeks. Algorithmic dose titration was performed to achieve a normal serum bicarbonate (HCO₃⁻) level of 22 to 29 mEq/L. The primary end point of interest was the between-group comparison of the proportion of patients with a ≥4 mEq/L increase in serum HCO₃⁻, or a normal serum HCO₃⁻, at week 12. The change from baseline in serum HCO₃⁻ was a secondary end point. There were two exploratory endpoints evaluating the effects of acidosis correction on physical functioning (measured by the Kidney Disease Quality of Life Short Form-36 Physical Functioning subscale) and a timed repeated chair stand test.

Mean baseline serum HCO₃⁻ was 17.3 mEq/L and mean baseline estimated glomerular filtration rate was 28.6 mL/min/1.73 m². Of the 217 patients, 96% completed the study. Comorbidities were hypertension (97%), diabetes (65%), left ventricular hypertrophy (44%), and congestive heart failure (11%).

The primary end point response definition was met by 59.2% of patients in the TRC101 group compared with 22.5% of those in the placebo group (P<.001). Mean serum HCO₃⁻ increased 4.5 mEq/L in the TRC101 group versus 1.7 mEq/L in the placebo group (P<.001). There were no significant differences in biochemical parameters between the excluded patients and the remaining patients; diabetes mellitus and serum high-sensitivity C-reactive protein (hs-CRP) were significantly higher in the excluded group compared with the remaining group (P=.006 and P=.004, respectively).

There was no effect on creatinine or other electrolytes. Adverse events occurred in 9.7% of patients in the placebo group and 13.7% of patients in the TRC101 group; most of the adverse events were gastrointestinal.

“TRC101 effectively and safely treated metabolic acidosis and improved self-reported physical functioning in CKD patients,” the researchers said.


This study was funded by Tricida, Inc.
ACEI or ARB use is associated with improved outcomes following hospitalization in patients with AKI. Results of the study were reported online in JAMA Internal Medicine [doi:10.1001/jamainternmed.2018.4749]. The study utilized data from the Alberta [Canada] Kidney Disease Network population-based database to identify patients ≥18 years of age residing in Alberta who were admitted to the hospital between July 1, 2008, and March 31, 2011, and had an episode of AKI during hospitalization.

Inclusion criteria were at least one outpatient serum creatinine measurement within 180 days prior to hospital admission to establish baseline kidney function, and one or more measurements during hospitalization to establish AKI. Among patients with more than one hospitalization during the study period, the first (index) was the only hospitalization to occur during the study period. Following application of inclusion and exclusion criteria, the study cohort included 46,253 patients. Mean age was 68.6 years, 52.8% (n=24,436) were male, and 85.9% (n=39,738) resided in an urban location; 50.6% (n=23,407) had prior CKD. The mean number of hospitalizations during the 3 years prior to the index hospitalization was 1.4; 17.0% (n=7849) had a cardiac diagnostic code as the primary diagnosis for the hospitalization. Most (75.9%, n=35,104) had hypertension, 38.2% (n=17,657) diabetes, 29.2% (n=13,499) had heart disease, and 20.9% (n=9690) had a history of stroke or transient ischemic attack. In all, 54.5% (n=25,211) of patients were using an ACEI or ARB within 6 months prior to the index hospitalization; 48.0% (n=22,193) were using an ACEI or ARB 6 months after discharge. Thirty-eight percent (n=17,852) never used an ACEI or ARB; 6.9% (n=3190) received a new prescription within 6 months following discharge. Forty-one percent (n=19,005) continued using an ACEI or ARB within 6 months after discharge, and 13.4% (n=620) of previous users did not restart use of an ACEI or ARB following discharge.

Of the total cohort, 9456 patients were matched 1:1 with similar patients who had no dispensed ACEI or ARB prescription within 6 months following discharge, resulting in a matched cohort of 18,912 patients. In the matched analysis, the adjusted hazard ratio (HR) for mortality associated with ACEI or ARB use after hospital discharge compared with no ACEI or ARB use was 0.85 (95% confidence interval [CI], 0.81-0.89).

There was an association between ACEI or ARB use with higher risk of renal-related hospitalization (acute renal failure, congestive heart failure, and hyperkalemia) (HR, 1.28; 95% CI, 1.12-1.46). There was no association between ACEI or ARB use and progression to ESRD or between ACEI or ARB use and the composite end point of progression to ESRD or sustained doubling of serum creatinine concentration.

Both new ACEI or ARB use (HR, 0.85; 95% CI, 0.78-0.93) and continued ACEI or ARB use (HR, 0.77; 95% CI, 0.73-0.80) after hospital discharge were associated with lower mortality compared with no ACEI or ARB use. Conversely, there was an association between stopping use of an ACEI or ARB prescribed prior to hospital admission and increased mortality (HR, 1.23; 95% CI, 1.17-1.30). In patients who were prescribed a new ACEI or ARB or who continued use of an ACEI or ARB after discharge, rates of renal-related hospitalization were higher than in patients with no ACEI or ARB use.

The researchers cited some limitations to the analysis, including the retrospective use of administrative and laboratory data and the observational design. In summary, the researchers said, “We found that the use of an ACEI or ARB in patients with AKI after hospital discharge was associated with lower mortality but a higher rate of hospitalization for a renal cause. This observation requires further evaluation in prospective studies evaluating postdischarge care strategies for patients with AKI. In particular, our results suggest a need for a trial to evaluate treatment with an ACEI or ARB in patients with AKI to determine whether this intervention improves long-term outcomes in high-risk patients.”

Fluid Management Quality Improvement Project Using Relative Blood Volume Monitoring

San Diego—Patients receiving hemodialysis at 20 Renal Research Institute clinics participated in a 1-year fluid management quality improvement (QI) project utilizing relative blood volume monitoring (RBV-M). Paul Balter, MD, and colleagues conducted a retrospective database analysis to examine changes in body weight and blood pressure in the participating patients. Results of the analysis were reported during a poster session at Kidney Week 2018 in a poster titled “Reduction in mean patient body weights and blood pressures were observed during a Fluids Management Quality Improvement (QI) Project Utilizing Relative Blood Volume Monitoring (RBV-M).”

Eligible patients received hemodialysis in the month prior to the QI project (pre-QI) and in the month at the end of the project. RBV-M was used to monitor relative blood volume during hemodialysis with Crit-Line® Monitors (CLM-III, CLM-IV, or CLC). For each patient, all available pre-hemodialysis and post-hemodialysis body weights and systolic and diastolic blood pressures were averaged monthly. The researchers conducted a subgroup analysis of patients with pre-QI hypertension; patients with pre-hemodialysis systolic blood pressure of 130 mmHg and/or pre-hemodialysis diastolic blood pressure of 80 mmHg during the pre-QI period were included in the subanalysis. Paired t-tests were used to test for differences between pre-QI and QI month 12.

A total of 653 patients were included in the analysis of those 473 had pre-QI hypertension. From pre-QI to QI month 12, mean pre-hemodialysis weight decreased from 84.06 kg to 83.27 kg (-0.79 kg, P=0.001) and post-hemodialysis weight decreased from 81.71 kg to 80.69 kg (-0.75 kg, P<0.05). Mean pre-hemodialysis systolic blood pressure decreased from 152.04 mmHg to 149.92 mmHg (-2.12 mmHg, P=0.005) and mean post-hemodialysis systolic blood pressure decreased from 139.32 mmHg to 137.09 mmHg (-2.23 mmHg, P=0.03). During the study period, mean pre-hemodialysis diastolic blood pressure decreased from 80.07 mmHg to 78.70 mmHg (-1.37 mmHg, P=0.002) and post-hemodialysis diastolic blood pressure decreased from 73.69 mmHg to 72.41 mmHg (-1.28 mmHg, P=0.003).

In the subgroup analysis of patients with hypertension during the pre-QI period, on average pre-hemodialysis systolic blood pressure decreased from 161.54 mmHg to 156.55 mmHg (-4.99 mmHg, P=0.001) and post-hemodialysis systolic blood pressure decreased from 145.56 mmHg to 141.56 mmHg (-4.00 mmHg, P=0.001).

In conclusion, the researchers said, “A QI project on fluid management utilizing RBV-M was associated with reductions in patient body weights and blood pressures. Most patients had pre-QI hypertension (73%). These patients had an average decrease in pre-hemodialysis systolic blood pressure of 4.99 mmHg and may be a population that could particularly benefit from a QI initiative on fluid management.”

Source: Balter P, Li Y, Mullen C, Kosmann GJ, Fico, Vella I. Reduction in mean patient body weights and blood pressures were observed during a Fluids Management Quality Improvement (QI) project utilizing relative blood volume monitoring (RBV-M). Abstract of a poster ([G-00367]) presented at the American Society of Nephrology Kidney Week 2018, October 26-26, 2018, San Diego, California.

Funding for this analysis was provided by Fresenius Medical Care Renal Therapies Group.
Supplementation with Omega-3 Polyunsaturated Fatty Acids to Prevent Vascular Access Failure

Worldwide, the most common renal replacement therapy is hemodialysis, best performed using a functioning arteriovenous vascular access; establishing and maintaining functional arteriovenous vascular access remains a major challenge associated with dialysis care. Dysfunction of arteriovenous fistula (AVF) and graft (AVG) leads to prolonged use of central venous catheters and is associated with repeat hospitalization and procedures as well as higher rates of complications and mortality.

The pathogenesis of arteriovenous access failure is complex and not well understood. Possible explanations include neointimal hyperplasia formation and impaired vascular remodeling, with insufficient vasodilation and vessel wall thickening in response to the increased pressure, shear stress, and oxygen tension that results from redirected arterial flow. Researchers, led by Andrea K. Viecelli, MD, hypothesized that access outcomes might be improved with omega-3 polyunsaturated fatty acids (omega-3 PUFAs) via pleiotropic effects on access maturation and function. However, there may also be an association between omega-3 PUFAs and bleeding complications in the patients with end-stage renal disease (ESRD) requiring hemodialysis.

To test the hypothesis and evaluate the benefits and harms of omega-3 PUFAs over placebo or no treatment for prevention of AVF or AVG failure, the researchers conducted a systematic review and meta-analysis. Results were reported in the American Journal of Kidney Diseases [2018;72(1):50-61].

The review included a search of MEDLINE (1946 through January 24, 2017); Embase (1980 through January 24, 2017); and the Cochrane Central Register of Controlled Trials (through issue 11 of 12, 2016). Eligible trials were randomized controlled and quasi-randomized controlled trials examining treatment with omega-3 polyunsaturated fatty acids (PUFAs) for arteriovenous access outcomes.

Supplementation with omega-3 PUFAs likely protects against primary loss of arteriovenous access patency; there may be little or no effect on dialysis suitability failure, access interventions, or access abandonment.

In conclusion, the researchers said, “Omega-3 PUFAs supplementation started at the time of arteriovenous access surgery, probably prevents primary patency loss within 12 months but may have little or no effect on access interventions, dialysis suitability failure, or access abandonment, and treatment harms are uncertain. Larger randomized controlled trials are required to determine the efficacy and safety of omega-3 PUFAs supplementation in patients requiring hemodialysis and to assess novel putative interventions to improve dialysis vascular outcomes. Based on the available evidence, recommendations on the routine use of omega-3 PUFAs for safely preventing arteriovenous access complications cannot be made.”
Self-management is required of patients with chronic diseases to limit disease progression, including regular monitoring visits for provider assessment, feedback, and adjustments to the care plan. These self-management directives involve a shift from passive to active disease management for the patient and require shifts in provider to patient communication approaches. Enabling higher levels of patient engagement can be informed by awareness of how patients discuss their encounters with providers.

Ann E. Vandenber, PhD, MPH, and colleagues conducted a qualitative study at the Atlanta Veterans Affairs (VA) renal clinic to analyze patient discourse on ongoing chronic kidney disease (CKD) monitoring encounters for health communication strategies that motivate patient engagement. Results of the study were reported online in *BMC Nephrology* [doi.org/10.1186/s12882-018-0981-7](doi.org/10.1186/s12882-018-0981-7).

The researchers extracted passages regarding CKD monitoring from transcripts of six focus groups on self-management. The transcripts represented 30 participants 70 years of age from the Atlanta VA renal clinic across three different CKD trajectories (stable, linear decline, and nonlinear). The extracted passages were examined using three-stage critical discourse analysis (description, interpretation, explanation) for recurring patterns across groups.

The average age of the participants was 75.1 years, 96.7% were male, and 60% were black. Inadequate health literacy ranged from 20% in the linear decline group to 27.3% in the non-linear trajectory group. There were 85 passages on physician-patient monitoring encounters. The views expressed by the patients with CKD were predominantly negative.

The comments indicated that the encounters left the patients in a state of limbo, and made them wary about their diagnosis and the factors that led to development of CKD. Positive exchanges, the comments said, were committed to monitoring and self-management important to “preserve what you’ve got with the kidney function you do have; it doesn’t get any better but at least you try to keep it from getting worse.” In positive exchanges, the provider is viewed as aligned with the patient’s goal to stabilize and protect the kidney. This alignment is viewed as comprehensible to the patients in these discussions.

In discussions of positive communications, the veterans defined positive exchanges as comprehensible. Some of the veterans said they were committed to monitoring and self-management because they understood the purpose of it. A participant in the stable trajectory group said that monitoring and self-management were important to “preserve what you’ve got with the kidney function you do have; it doesn’t get any better but at least you try to keep it from getting worse.” In positive exchanges, the provider is viewed as aligned with the patient’s goal to stabilize and protect the kidney. This alignment is viewed as comprehensible to the patients in these discussions.

The researchers reported a number of inherent limitations to the study, including the data being analyzed by a single investigator, the subjective nature of discourse analysis, and limiting the study to one VA site.

In conclusion, the authors said, “CKD patients” need for both comprehensible information and for reciprocity in the monitoring encounter may best be supported by maximizing positive communication through provider messages that emphasize kidney protection and by minimizing perceptions of unequal exchange by providing consistent and contextualized information about CKD monitoring results during each monitoring encounter.”

**Patient Perspectives on Chronic Kidney Disease Monitoring and Self-Management**

Patients in each of the trajectory groups indicated that they felt left out of the communication loop between his nephrologist and primary care provider. He added that the “doctor provides little” in exchange for his time and effort.

In further discussions of unfair exchanges, the veterans described providers using terms such as powerful, apathetic, or disengaged (withholding of information during monitoring encounters). Patients in each of the groups cited hearing the unhelpful phrase “keep doing what you’re doing.” The veterans felt that approach put the burden entirely on the patients, without the skills or experience to obtain information on their own.

Descriptions of the negative and incomprehensible monitoring encounters described them as an unequal exchange between the patient and the provider. This theme could be viewed from the separate roles of patient and provider.

For one patient in the group with linear CKD decline, the basic features of monitoring were regular periodic visits to a nephrologist, blood draws for creatinine testing, and urine samples for albumin testing. One factor leading to the patient’s perception of an unequal exchange was delayed communication regarding results of the testing. A patient in the stable CKD trajectory group described the monitoring experience as repeated visits where he received numeric results of the laboratory testing; the patient felt the information was inadequate as presented. A patient in the non-linear CKD trajectory group indicated that he felt left out of the communication loop between his nephrologist and primary care provider. He added that the “doctor provides little” in exchange for his time and effort.

In further discussions of unfair exchanges, the veterans described providers using terms such as powerful, apathetic, or disengaged (withholding of information during monitoring encounters). Patients in each of the groups cited hearing the unhelpful phrase “keep doing what you’re doing.” The veterans felt that approach put the burden entirely on the patients, without the skills or experience to obtain information on their own.

Fragmented care was also raised as a factor that blocked coherence and progress of disease management. Two patients in the linear CKD decline group said that CKD monitoring is part of care for multiple chronic conditions and that they were shuttled between various providers and treatments.

In discussions of positive communications, the veterans defined positive exchanges as comprehensible. Some of the veterans said they were committed to monitoring and self-management because they understood the purpose of it. A participant in the stable trajectory group said that monitoring and self-management were important to “preserve what you’ve got with the kidney function you do have; it doesn’t get any better but at least you try to keep it from getting worse.” In positive exchanges, the provider is viewed as aligned with the patient’s goal to stabilize and protect the kidney. This alignment is viewed as comprehensible to the patients in these discussions.

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By authors of *BMC Nephrology* [doi.org/10.1186/s12882-018-0981-7](doi.org/10.1186/s12882-018-0981-7).*
Temporal Artery Thermometer versus Hemodialysis Machine Internal Blood Monitoring

In many hemodialysis units, measuring pre-dialysis body temperature is a routine part of care. The gold standard for measurement of body temperature is the temperature of central (core) blood; however, in the majority of clinical settings, it is not feasible to use core blood temperature. In most cases, temperature is measured at other sites, such as oral, axillary, tympanic, or temporal artery.

Core temperature readings can be displayed on modern hemodialysis machines equipped with an internal blood temperature monitor, yet many dialysis units record manual temperatures using peripheral thermometers. According to Meaghan Lunney, MSc, and colleagues, this practice may be unnecessary and may also be prone to error. To compare body temperature measured by hemodialysis machine thermometers with those measured by temporal artery thermometer, the researchers conducted a prospective cross-sectional study. The researchers also sought to examine the feasibility of replacing the currently used arterial method with dialysis machine thermometers. Results of the study were reported online in *BMC Nephrology* [doi.org/10.1186/s12882-018-0938-x].

The primary outcome of interest was body temperature. Secondary outcomes were whether mean temperature varied depending on self-reported patient characteristics such as sex, age, duration of dialysis, and diabetes. Core temperature readings can be distributed. The mean temperature measured by the temporal artery thermometer was 36.7 °C compared with the mean dialysis machine temperature of 36.42 °C, a significant difference (P<.001). The mean difference between the temporal artery measurement and the dialysis machine measurement was 0.27 °C (95% confidence interval, 0.18-0.37). Three of the 94 observations were outside the limits of 95% agreement by the Bland-Altman agreement test. Using the temporal artery thermometers, two of the 94 patients (2.1%) had temperatures below 36 °C; using the dialysis machine thermometer, 12 of the 94 (12.8%) had temperatures below 36 °C.

In sensitivity analysis comparing only the first pairs of temperature measurement within the first 15 minutes of treatment, there were no statistical differences in mean body temperature among the hemodialysis patients as measured by a temporal artery thermometer and those without diabetes (36.33 °C vs 36.52 °C, respectively; P=.02). There was a significant difference between the temperature of patients with diabetes and those without diabetes (36.33 °C vs 36.52 °C, respectively; P=.02).

The researchers cited some potential limitations to the study, including having different nurses involved in the data collections; the inability to obtain both temperature measurements during the first 15 minutes of dialysis treatment in seven of the 94 patients; the possibility that the findings are not generalizable to patients with significant access recirculation; and not including febrile patients in the study.

“The mean body temperature of hemodialysis patients as measured by a temporal artery thermometer was 0.27 °C higher than the mean core temperature measured by the dialysis machine. As core temperature is the gold standard, using the dialysis machine to measure body temperature in hemodialysis patients rather than an external thermometer may result in slightly greater accuracy while possibly also lowering staff workload,” the researchers said.
Dialysis Therapy Associated with Withdrawal from High Comorbid Condition Burden

Over the past decade, annual rates of dialysis therapy initiation have been relatively stable. Dialysis patients are living longer than before, creating an interest in issues such as conservative care for end-stage renal disease (ESRD), palliative care in nephrology, and withdrawal from dialysis therapy. Withdrawal from dialysis therapy is a cause of death in -10% to 20% of patients in western countries and seems to be increasing. There are few data available on differences in clinical outcomes between patients on maintenance dialysis who do and do not withdraw from dialysis therapy.

James B. Wetmore, MD, MS, and colleagues conducted a case-control analysis to examine clinical events in the period preceding withdrawal in patients on maintenance dialysis. The study examined rates of medical events, time spent in the hospital and in skilled nursing facilities, and putative markers of morbidity; data were drawn in part from claims for durable medical equipment use in the period preceding withdrawal to assess differences in patients who withdraw and those who do not withdraw. The researchers sought to test the hypothesis that the period before withdrawal would be characterized by increasing rates of medical events, institutionalization, and other markers potentially signaling morbidity. Results of the study were reported in the American Journal of Kidney Diseases [2018;71(6):831-841].

The study utilized the US Renal Data System ESRD Medical Evidence Report, the ESRD Death Notification form, and Medicare Parts A and B claims. Medicare insures the majority of patients on maintenance dialysis; Medicare billing claims data were used to determine the presence of comorbid conditions, derive the Liu comorbidity index, and generate a putative marker of morbidity based on claims for durable medical equipment use.

Case patients were patients who withdrew from hemodialysis therapy between January 1, 2008, and December 31, 2011; for those patients, the researchers created an index date, defined as the date of withdrawal, for each patient who withdrew. For hemodialysis patients who did not withdraw, the researchers created their respective index dates, defined as the calendar date on which dialysis duration was within ±30 days of dialysis therapy duration among patients who withdrew.

Medical events included in the analysis were hospitalizations for myocardial infarction (MI), congestive heart failure, stroke, amputation/critical limb ischemia, sepsis, pneumonia, vascular access infection, gastrointestinal bleeding, or fracture. The subset of hospitalizations for MI, stroke, amputation/critical limb ischemia, sepsis, or fractures were deemed “major medical events.”

There were 96,814 patients who initiated maintenance hemodialysis on or before January 1, 2011, and withdrew January 1, 2008, through December 31, 2011. Of those, 18,412 survived at least 1 year on hemodialysis therapy, and had at least 9 months of Medicare Parts A and B coverage immediately preceding their respective index dates. Of those, 18,367 were adults of known race for whom comparable nonwithdrawal patients could be found on the basis of the index date. The 18,367 patients were the case patients for the match 1 analysis and the matches (n=220,443) were the controls.

Of the patients in the withdrawal group, 13,522 were randomly further matched in a 1:4 ratio with nonwithdrawers with similar age, sex, race, cause of ESRD, and duration of dialysis therapy as of the index date, resulting in 53,288 more fully matched nonwithdrawers (match 2 group). Among patients in the match 1 group, those who withdrew were older and more likely to be female, white than a minority race/ethnicity (71.8% vs 46.2%), and have longer duration of dialysis therapy (4.8 vs 4.5 years). In addition, patients who withdrew had higher comorbid conditions and morbidity scores. In the match 2 group, there were only slight differences in distributions of matched variables; however, patients who withdrew had generally higher comorbid condition burdens and higher morbidity scores.

In the match 1 group, there was an association between older age and withdrawal from dialysis. Compared with patients 65 to 74 years of age, adjusted odds ratios (ORs) for withdrawal were 1.61 (95% confidence interval [CI], 1.54-1.68) for patients 75 to 84 years of age and 2.68 (95% CI, 2.54-2.82) for those 285 years of age; the adjusted OR for patients 18 to 44 years of age was 0.36 (95% CI, 0.32-0.40).

Women were more likely to withdraw than men (adjusted OR, 1.07; 95% CI, 1.04-1.11). With the exception of Native Americans, compared with white patients, nonwhite patients had lower odds of withdrawal: adjusted ORs 0.36 (95% CI, 0.35-0.38) for blacks, 0.47 (95% CI, 0.42-0.53) for Asians, and 0.46 (95% CI, 0.44-0.49) for Hispanics. There was an association between longer duration of dialysis therapy and withdrawal, e.g., compared with duration of 3 to <4 years, adjusted ORs for withdrawal were 0.55 (95% CI, 0.52-0.58) for 1 to <2 years but 1.37 (95% CI, 1.30-1.44) for ≥2 years.

There was an association between hospital or skilled nursing facility stay and increased odds of withdrawal (1.01 per day of institutionalization). Higher morbidity score was associated with increased likelihood of withdrawal: compared with a score of 0, a score of 3 to 4 was associated with an adjusted OR of 3.48 (95% CI, 3.29-3.67), and a score of 7, with an adjusted OR of 12.10 (95% CI, 11.37-12.87).

Limitations cited by the authors included the inability to generalize the findings to populations other than US Medicare beneficiaries, and not including data on patients who withdrew <1 year following initiation of dialysis therapy.

“In conclusion, the period before dialysis therapy withdrawal was characterized by increasing rates of medical events and hospitalization. A marker of morbidity based on durable medical equipment use appears to be strongly associated with withdrawal, even after adjustment for a host of other factors. Men and members of certain minority groups, such as blacks, Asians, and Hispanics, were less likely to withdraw than women and whites. When they did withdraw, blacks and Hispanics were more likely than whites to withdraw in the hospital. Further work examining elective dialysis therapy withdrawal experience is warranted,” the researchers said.

TAKEAWAY POINTS

Researchers conducted a case-control analysis to examine differences in the clinical course between patients receiving maintenance dialysis who do and who do not withdraw from dialysis therapy.

- Older age (≥65 years) was associated with higher adjusted odds of withdrawal and patients who withdrew were more likely to be female and of white race.

- Patients with higher comorbid condition burden were more likely to withdraw from dialysis. There was an association between a higher durable medical equipment claims-based morbidity score and the odds of withdrawal: the association remained following adjustment for traditional comorbid scores and institutionalization.
Patients with Advanced CKD Describe Emotional Impact of Their Illness and Treatment

Patients with advanced chronic kidney disease (CKD) have a high symptom burden and a high prevalence of comorbid conditions, as well as limited life expectancy. Studies designed to examine patients' healthcare experiences suggest that patient concerns can be opposed to those of providers. The Institute of Medicine defines patient-centered care as “care that is respectful of and responsive to individual patient preferences, needs, and values and [ensures] that patient values guide all clinical decisions.” There are data that indicate that for many patients with advanced CKD, major treatment decisions, including whether and when to initiate dialysis, are commonly influenced more by provider- and system-level considerations than by the goals and concerns of the patient.

Ann M. O’Hare, MD, and colleagues report on findings as part of a study on advance care planning among patients with advanced CKD that illuminate the illness experiences in that patient population, patients’ interactions with providers and the healthcare system, and their thoughts on advance care planning and care at the end of life. The researchers provided insights into the emotional impact of illness and care in these patients. The findings were reported in the Clinical Journal of the American Society of Nephrology (2018;13:1022-1029).

The single-center study on advance care planning enrolled patients receiving care in the nephrology clinic or dialysis unit at the Veterans Administration Puget Sound Health Care System in Seattle, Washington. Inclusion criteria were estimated glomerular filtration rate ≤20 mL/min/1.73 m² on at least two occasions 3 months apart or undergoing treatment with maintenance dialysis. Study participants completed a 45- to 60-minute semistructured, one-on-one interview that included general questions about their illness experience and encounters with providers and the healthcare system as well as specific questions about their experience and perspectives on advance care planning.

Of the 56 patients with advanced CKD who received an invitation to participate in the study via mail, 27 (48%) enrolled. Mean age of enrolled patients was 62 years, 96% were men, and most self-identified as white (56%), 33% as black, and 11% as other race. At the time of the interview, 10 patients (37%) were receiving hemodialysis, five (19%) were receiving peritoneal dialysis, and 12 (44%) had not initiated dialysis.

The researchers identified three emergent themes related to patients' emotional experiences of care and illness: (1) the emotional impact of interactions with individual providers; (2) the emotional impact of encounters with the healthcare system; and (3) the emotional impact of making sense of their illness experiences.

When providers did not appear to be concerned with patients' experiences of illness, patients could feel a sense of mistrust, abandonment, isolation, and/or alienation; those same feelings could arise as a result of dealing with the healthcare system. In dealing with making sense of their illness, patients often worked to apportion blame, sometimes feeling personally responsible for the course of their illness. Further, patients sometimes relied on counterfactual explanations for their conditions.

One participant described feeling alienated when his provider ordered a kidney biopsy. The patient had a pinched nerve that would make the biopsy procedure dangerous and difficult and he felt the provider was not seeing him as a whole person and did not understand his specific situation. Mistrust was often expressed as providers not informing patients about worsening kidney function associated with progression of CKD. Some participants described positive relationships with providers, while others felt their providers had little to offer beyond standard treatments and procedures, leaving them feeling abandoned and alone.

Patients were also emotionally affected by encounters with the healthcare system. When providers moved in and out of patients' care during the course of treatment, the patient often felt a sense of mistrust. Further, discontinuity of care was perceived by some patients as contributing to their course of illness. Patients experienced a great deal of distress when providers did not work collaboratively with their colleagues.

Emotional toll was sometimes the result of seemingly mundane aspects of healthcare delivery. For example, one man who met with several providers on the same team at a day-long visit was not told until the last visit, with the nephrologist, that his renal prognosis was worse than anticipated. He was left feeling “alone and isolated” because at the end of the day he came to realize that “all [of the providers] knew my kidney function had decreased, but no one had told me.”

In addressing the survey questions on making sense of their illness, patients expressed difficulty with the question of whether and to what extent they were responsible for the course of their kidney disease. They were quick to assign blame, often blaming themselves and assuming that their kidney disease could have been prevented.

There were some limitations to the findings, including the single-center design of the study, which raises the question of transferability of the findings and the potential for bias; the small percentage of women participants; and limiting the participants to those who could provide informed consent.

In conclusion, the researchers said, “Interactions with individual providers and with the wider health system coupled with patients' own struggle to make meaning of their illness can take a large emotional toll. Our findings suggest that a deeper appreciation of patients' emotional experiences may offer important opportunities to improve care and highlight the need for more in-depth work in this area.”
Germline Mutations May be Prevalent in Patients with Renal Cell Carcinoma

Renal cell carcinoma (RCC) affects approximately 64,000 patients in the United States every year; it is one of the ten most frequently diagnosed cancers nationwide. On initial diagnosis, approximately 30% of patients present with locoregional (stage III) or metastatic disease. Clear cell RCC (ccRCC) is the most common subtype of RCC and is characterized by loss of function of the von Hippel-Lindau (VHL) protein. Non-clear cell RCCs (nccRCCs) include papillary type I and II, chromophobe, microphthlamia transcription factor family translocation associated, collecting duct, medullary, and other rare subtypes. There are several autosomal dominant inherited cancer syndromes that predispose patients to ccRCC and nccRCC, which are thought to account for 5% of all cases. However, according to Maria I. Carlo, MD, and colleagues, those estimates have been derived mainly from early-stage RCC and there have been no studies looking specifically at advanced disease.

Dr. Carlo et al. conducted a cohort study to examine the frequency of germline mutations in 76 cancer-associated genes in patients with advanced RCC. The study participants were unselected for inherited syndrome risk factors, including age at onset, multifocal disease, or family history. The researchers sought to assess the prevalence of germline mutations in known RCC predisposition genes and other cancer-associated genes and to identify clinical and pathologic factors associated with germline mutations. Results of the study were reported online in JAMA Oncology [doi:10.1001/jamaoncol.2018.1986].

The study was conducted from October 1, 2015, to July 31, 2017. The main outcomes were mutation prevalence and spectrum in patients with advanced RCC. Clinical characteristics were assessed by mutation status. Of the 267 patients with advanced (American Joint Committee on Cancer stage III or IV) RCC seen in medical oncology or urology clinics at Memorial Sloan Kettering Cancer Center were offered germline sequencing and disclosure of results.

Of the 267 patients who consented to tumor-normal testing with MSK-IMPACT (Memorial Sloan Kettering-Integrated Mutation Profiling of Actionable Cancer Targets), 95.1% (n=254) consented to receive the germline results. Of the 254, median age was 56 years, 179 (70.5%) were male and 75 (29.5%) were female, and 211 (83.1%) were non-Hispanic white.

Of the 254 patients opting to receive results, 177 had ccRCC (69.7%), 74 had nccRCC (29.1%), and three (1.2%) had both. Thirty-three patients had a history of a second malignant tumor, excluding non-melanoma skin cancers. The most frequent secondary tumors were prostate (n=8), breast (n=4), and melanoma (n=3). Fourteen patients had bilateral or multifocal disease. and 24 reported a family history of RCC.

Forty-one patients carried pathogenic or likely pathogenic germline variants in 17 different cancer-predisposition genes.

Forty-one patients carried pathogenic or likely pathogenic germline variants in 17 different cancer-predisposition genes. None of the cohort had more than one germline mutation. Fourteen patients carried mutations in RCC-associated genes, and 27 carried mutations in genes not clearly associated with RCC. Of the 41 patients, 17 carried mutations of high penetrance, nine of moderate penetrance, 12 of low penetrance or uncertain clinical actionability, and three in genes linked to autosomal recessive syndromes.

Of the 177 patients with ccRCC, 25 (14.1%) had a germline mutation and three in a gene associated with RCC. Among patients with nccRCC (n=74), 13 had a germline mutation, nine in a gene associated with RCC. All three of the patients with both ccRCC and nccRCC had germline mutations. The researchers conducted analyses to assess the prevalence of mutations among patients identified as at higher risk for inherited syndromes, such as patients with a family history of RCC, early onset (defined as ≤46 years of age), and multifocal disease at diagnosis. Those with nccRCC or multifocal RCC were significantly more likely to have an RCC-associated mutation. Seven patients had germline FH mutations indicative of the hereditary syndrome HRCC (he-reditary leiomyomatosis RCC); all patients had tumors of unclassified histologic type or identified as FH deficient.

Median age at diagnosis for FH-positive patients was 49 years; four presented with metastatic disease and three later developed metastatic disease. None had multifocal RCC or a family history of RCC.

Ninety-nine patients would have met American College of Medical Genetics criteria for clinical genetics referral. Of the 14 patients with mutations associated with RCC, five would not have met referral criteria. Of the 12 patients with high or moderate penetrance mutations not related

Takeaway Points

- Researchers at Memorial Sloan Kettering Cancer Center conducted a cohort study to assess the prevalence of cancer-related germline mutations in patients with advanced renal cell carcinoma (RCC).
- The cohort included 264 patients of those 5.3% had mutations in syndromic RCC-associated genes, and 10.5% had mutations in other cancer-associated genes.
- Germline mutations may be more frequent in patients with advanced non-clear cell RCC.

Nephrology Times | January/February 2019
Only one calcimimetic lowers and maintains key sHPT lab values with IV administration you control¹

Indication
Parsabiv™ (etelcalcetide) is indicated for the treatment of secondary hyperparathyroidism (HPT) in adult patients with chronic kidney disease (CKD) on hemodialysis.

Limitations of Use:
Parsabiv™ has not been studied in adult patients with parathyroid carcinoma, primary hyperparathyroidism, or with CKD who are not on hemodialysis and is not recommended for use in these populations.

Important Safety Information
Contraindication: Parsabiv™ is contraindicated in patients with known hypersensitivity to etelcalcetide or any of its excipients. Hypersensitivity reactions, including pruritic rash, urticaria, and face edema, have occurred.

Hypocalcemia: Parsabiv™ lowers serum calcium and can lead to hypocalcemia, sometimes severe. Significant lowering of serum calcium can cause QT interval prolongation and ventricular arrhythmia. Patients with conditions that predispose to QT interval prolongation and ventricular arrhythmia may be at increased risk for QT interval prolongation and ventricular arrhythmias if they develop hypocalcemia due to Parsabiv™. Closely monitor corrected serum calcium and QT interval in patients at risk on Parsabiv™.

Significant reductions in corrected serum calcium may lower the threshold for seizures. Patients with a history of seizure disorder may be at increased risk for seizures if they develop hypocalcemia due to Parsabiv™. Monitor corrected serum calcium in patients with seizure disorders on Parsabiv™.

Concurrent administration of Parsabiv™ with another oral calcimimetic could result in severe, life-threatening hypocalcemia. Patients switching from cinacalcet to Parsabiv™ should discontinue cinacalcet for at least 7 days prior to initiating Parsabiv™. Closely monitor corrected serum calcium in patients receiving Parsabiv™ and concomitant therapies known to lower serum calcium.

Measure corrected serum calcium prior to initiation of Parsabiv™. Do not initiate in patients if the corrected serum calcium is less than the lower limit of normal. Monitor corrected serum calcium within 1 week after initiation or dose adjustment and every 4 weeks during treatment with Parsabiv™. Measure PTH 4 weeks after initiation or dose adjustment of Parsabiv™. Once the maintenance dose has been established, measure PTH per clinical practice.

Worsening Heart Failure: In Parsabiv™ clinical studies, cases of hypotension, congestive heart failure, and decreased myocardial performance have been reported. Closely monitor patients treated with Parsabiv™ for worsening signs and symptoms of heart failure.

Upper Gastrointestinal Bleeding: In clinical studies, 2 patients treated with Parsabiv™ in 1253 patient years of exposure had upper gastrointestinal (GI) bleeding at the time of death. The exact cause of GI bleeding in these patients is unknown and there were too few cases to determine whether these cases were related to Parsabiv™.

Patients with risk factors for upper GI bleeding, such as known gastritis, esophagitis, ulcers or severe vomiting, may be at increased risk for GI bleeding with Parsabiv™. Monitor patients for worsening signs and symptoms of GI bleeding and ulcerations during Parsabiv™ therapy.

Adynamic Bone: Adynamic bone may develop if PTH levels are chronically suppressed.

Adverse Reactions: In clinical trials of patients with secondary HPT comparing Parsabiv™ to placebo, the most common adverse reactions were blood calcium decreased (64% vs. 10%), muscle spasms (12% vs. 7%), diarrhea (11% vs. 9%), nausea (11% vs. 6%), vomiting (9% vs. 5%), headache (8% vs. 6%), hypocalcemia (7% vs. 0.2%), and paresthesia (6% vs. 1%).

Please see Brief Summary of full Prescribing Information on adjacent page.

¹ IV = intravenous; sHPT = secondary hyperparathyroidism; PTH = parathyroid hormone; P = phosphate; cCa = corrected calcium.

Reference: 1. Parsabiv™ (etelcalcetide) prescribing information, Amgen.
for worsening signs and symptoms of heart failure.

could not be completely excluded. Closely monitor patients treated with PARSABIV.

1% of placebo-treated patients. Reductions in corrected serum calcium may be

due to initiating PARSABIV and concomitant therapies known to lower serum calcium.

significant reductions in corrected serum calcium may lower the threshold for

seizures. Patients with a history of seizure disorder may be at increased risk for

seizures if they develop hypocalcemia due to PARSABIV. Closely monitor corrected serum calcium

and QT interval in patients at risk receiving PARSABIV.

Significant lowering of serum calcium can cause paresthesias, myalgias, muscle

spasms, seizures, QT interval prolongation, and ventricular arrhythmia.

QT Interval Prolongation and Ventricular Arrhythmia

In clinical studies, two patients treated with PARSABIV in 1253 patient-years of

exposure had upper gastrointestinal (GI) bleeding noted at the time of death while

no patient in the control groups in 384 patient-years of exposure had upper GI

bleeding noted at the time of death. The exact cause of GI bleeding in these patients

is unknown, and there were too few cases to determine whether these cases were

related to PARSABIV.

Patients with risk factors for upper GI bleeding (such as known gastritis, esophagitis, ulcers, or severe vomiting) may be at increased risk for GI bleeding while receiving PARSABIV treatment. Monitor patients for worsening of common GI adverse reactions of nausea and vomiting associated with PARSABIV.[see Adverse Reactions (6.1) in PARSABIV full prescribing information] and for signs and symptoms of GI bleeding and ulcerations during PARSABIV therapy. Promptly evaluate and treat any suspected GI bleeding.

Adynamic Bone

Adynamic bone may develop if PTH levels are chronically suppressed. If PTH levels decrease below the recommended target range, the dose of vitamin D sterols and/or PARSABIV should be reduced or therapy discontinued. After discontinuation, resume therapy at a lower dose to maintain PTH levels in the target range [see Dosage and Administration (2.7) in PARSABIV full prescribing information].

ADVERSE REACTIONS

The following adverse reactions are described in greater detail in other sections of the labeling:

• Hypocalcemia [see Warnings and Precautions (5.1) in PARSABIV full prescribing information]

• Worsening Heart Failure [see Warnings and Precautions (5.2) in PARSABIV full prescribing information]

• Upper Gastrointestinal Bleeding [see Warnings and Precautions (5.3) in PARSABIV full prescribing information]

• Adynamic Bone [see Warnings and Precautions (5.4) in PARSABIV full prescribing information]

Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared with rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

The data in Table 2 are derived from two placebo-controlled clinical studies in patients with chronic kidney disease and secondary hyperparathyroidism on hemodialysis. The data reflect exposure of 503 patients to PARSABIV with a mean duration of exposure to PARSABIV of 23.6 weeks. The mean age of patients was approximately 58 years, and 60% of the patients were male. Of the total patients, 67% were Caucasian, 26% were Black or African American, 2.6% were Asian, 1.2% were Native Hawaiian or Other Pacific Islander, and 1.6% were categorized as Other.

Table 2 shows common adverse reactions associated with the use of PARSABIV in the pool of placebo-controlled studies. These adverse reactions occurred more commonly on PARSABIV than on placebo and were reported in at least 5% of patients treated with PARSABIV.

Table 2: Adverse Reactions Reported in ≥ 5% of PARSABIV-Treated Patients

<table>
<thead>
<tr>
<th>Adverse Reaction*</th>
<th>Placebo (N = 513)</th>
<th>PARSABIV (N = 503)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood calcium decreased*</td>
<td>10%</td>
<td>64%</td>
</tr>
<tr>
<td>Muscle spasms</td>
<td>7%</td>
<td>12%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>9%</td>
<td>11%</td>
</tr>
<tr>
<td>Nausea</td>
<td>6%</td>
<td>11%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>5%</td>
<td>9%</td>
</tr>
<tr>
<td>Headache</td>
<td>6%</td>
<td>8%</td>
</tr>
<tr>
<td>Hypocalcemia</td>
<td>0.2%</td>
<td>7%</td>
</tr>
<tr>
<td>Paresthesia*</td>
<td>1%</td>
<td>6%</td>
</tr>
</tbody>
</table>

*Included adverse reactions reported with at least 1% greater incidence in the PARSABIV group compared to the placebo group.

* Asymptomatic reductions in calcium below 7.5 mg/dL or clinically significant asymptomatic reductions in corrected serum calcium between 7.5 and < 8.3 mg/dL (that required medical management)

* Paresthesia includes preferred terms of paresthesia and hypesthesia
Other adverse reactions associated with the use of PARSABIV but reported in < 5% of patients in the PARSABIV group in the two placebo-controlled clinical studies were:

- Hyperkalemia: 3% and 4% for placebo and PARSABIV, respectively.
- Hospitalization for Heart Failure: 1% and 2% for placebo and PARSABIV, respectively.
- Myalgia: 0.2% and 2% for placebo and PARSABIV, respectively.
- Hypophosphatemia: 0.2% and 1% for placebo and PARSABIV, respectively.

### Description of Selected Adverse Reactions

#### Hypocalcemia

In the combined placebo-controlled studies, a higher proportion of patients on PARSABIV developed at least one corrected serum calcium value below 7.0 mg/dL (7.6% PARSABIV, 3.1% placebo), below 7.5 mg/dL (27% PARSABIV, 5.5% placebo), and below 8.3 mg/dL (19% PARSABIV, 19% placebo). In the combined placebo-controlled studies, 1% of patients in the PARSABIV group and 0% of patients in the placebo group discontinued treatment due to an adverse reaction attributed to a low corrected serum calcium.

#### Hypophosphatemia

In the combined placebo-controlled studies, 19% of patients treated with PARSABIV and 8.2% of patients treated with placebo had at least one measured phosphorus level below the lower normal limit (i.e., 2.2 mg/dL). QTc Interval Prolongation Secondary to Hypocalcemia

In the combined placebo-controlled studies, more patients treated with PARSABIV experienced a maximum increase from baseline of greater than 60 msec in the QTcF interval (7.6% placebo versus 1.2% PARSABIV). The patient incidence of maximum post-baseline predialysis QTcF > 500 msec in the placebo and PARSABIV groups was 1.9% and 4.9%, respectively.

#### Hypersensitivity

In the combined placebo-controlled studies, the subject incidence of adverse reactions potentially related to hypersensitivity was 4.4% in the PARSABIV group and 3.7% in the placebo group. Hypersensitivity reactions in the PARSABIV group were pruritic rash, urticaria, and face edema.

### Immunogenicity

As with all peptide therapeutics, there is potential for immunogenicity. The detection of anti-drug binding antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody positivity in an assay may be influenced by several factors, including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to etelcalcetide with the incidence of antibodies to other products may be misleading.

In clinical studies, 7.1% (71 out of 995) of patients with secondary hyperparathyroidism treated with PARSABIV for up to 6 months tested positive for binding anti-etelcalcetide antibodies. Fifty-seven out of 71 had pre-existing hyperparathyroidism treated with PARSABIV for up to 6 months tested positive for etelcalcetide with the incidence of antibodies to other products may be misleading.

No evidence of altered pharmacokinetic profile, clinical response, or safety profile was associated with pre-existing or developing anti-etelcalcetide antibodies. If formation of anti-etelcalcetide binding antibodies with a clinically significant effect is suspected, contact Amgen at 1-800-77-AMGEN (1-800-772-6436) to discuss antibody testing.

### USE IN SPECIFIC POPULATIONS

#### Pregnancy

- **Risk Summary**

  There are no available data on the use of PARSABIV in pregnant women. In animal reproduction studies, effects were seen at doses associated with maternal toxicity that included hypocalcemia. In a pre- and post-natal study in rats administered etelcalcetide during organogenesis through delivery and weaning, there was a slight increase in perinatal pup mortality, delay in parturition, and transient effects on pup growth at exposures 1.8 times the human exposure for the clinical dose of 15 mg three times per week. There was no effect on sexual maturation, neurobehavioral, or reproductive function in the rat offspring. In embryo-fetal studies, when rats and rabbits were administered etelcalcetide during organogenesis, reduced fetal growth was observed at exposures 2.7 and 7 fold clinical exposures, respectively, there was reduced fetal growth associated with maternal toxicities of hypocalcemia, tremoring, and reductions in body weight and food consumption.

  In a pre- and post-natal development study in Sprague-Dawley rats administered etelcalcetide at 0.75, 1.5, and 3 mg/kg/day by the intravenous route (gestation day 7 to lactation day 20), there was a slight increase in perinatal pup mortality, delay in parturition, and transient reductions in post-natal growth at 3 mg/kg/day (representing 1.8-fold human exposures at the clinical dose of 15 mg three times per week based on AUC, associated with maternal toxicities of hypocalcemia, tremoring, and reductions in body weight and food consumption. There were no effects on sexual maturation, neurobehavioral, or reproductive function at up to 3 mg/kg/day, representing exposures up to 1.8-fold human exposure based on AUC.

- **Lactation**

  Risk Summary

  There are no data regarding the presence of PARSABIV in human milk or effects on the breastfed infant or on milk production. Studies in rats showed [14C]-etelcalcetide was present in the milk at concentrations similar to plasma. Because of the potential for PARSABIV to cause adverse effects in breastfed infants including hypocalcemia, advise women that use of PARSABIV is not recommended while breastfeeding.

- **Pediatric Use**

  The safety and efficacy of PARSABIV have not been established in pediatric patients.

- **Geriatric Use**

  Of the 503 patients in placebo-controlled studies who received PARSABIV, 177 patients (35.2%) were ≥ 65 years old and 72 patients (14%) were ≥ 75 years old. No clinically significant differences in safety or efficacy were observed between patients ≥ 65 years and younger patients (≥ 18 and < 65 years old). No differences in plasma concentrations of etelcalcetide were observed between patients ≥ 65 years and younger patients (≥ 18 and < 65 years old).

#### OVERDOSAGE

There is no clinical experience with PARSABIV overdosage. Overdosage of PARSABIV may lead to hypocalcemia with or without clinical symptoms and may require treatment. Although PARSABIV is cleared by dialysis, hemodialysis has not been studied as a treatment for PARSABIV overdosage. In the event of overdosage, corrected serum calcium should be checked and patients should be monitored for symptoms of hypocalcemia, and appropriate measures should be taken. [See Warnings and Precautions (5.1) in PARSABIV full prescribing information].

### Data

#### Animal Data

There were no effects on embryo-fetal development in Sprague-Dawley rats when etelcalcetide was dosed at 0.75, 1.5, and 3 mg/kg/day by the intravenous route during organogenesis (pre-mating to gestation day 17) at exposures up to 1.8 times human exposures at the clinical dose of 15 mg three times per week based on AUC. No effects on embryo-fetal development were observed in New Zealand White rabbits at doses of etelcalcetide of 0.375, 0.75, and 1.5 mg/kg/day by the intravenous route (gestation day 7 to 19), representing up to 4.3 times human exposures based on AUC. In separate studies at higher doses of 4.5 mg/kg in rats (gestation days 6 to 17) and 2.25 mg/kg in rabbits (gestation days 7 to 20), representing 2.7 and 7 fold clinical exposures, respectively, there was reduced fetal growth associated with maternal toxicities of hypocalcemia, tremoring, and reductions in body weight and food consumption.

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### AMGEN

Manufactured for:
KAI Pharmaceuticals, Inc., a wholly owned subsidiary of Amgen, Inc.
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Patent: http://pat.amgen.com/Parsabiv/

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Predictors of Early Technique Failure in Peritoneal Dialysis

Technique failure in peritoneal dialysis is a major complication of the modality and is associated with risk to patients. The first year on peritoneal dialysis is a particularly vulnerable period; just less than half of patients on peritoneal dialysis who experience technique failure do so within the first year of treatment. Published rates of early technique failure vary, but the rates range from 4.9% to 20.9%, and there have been consistent reports of the risk association with an early transfer to hemodialysis. Of the patients who switch to hemodialysis in the first year of treatment, >80% do so with a temporary vascular catheter; increasing the risk for infection, prolonged hospitalization, mortality, and increased health care costs.

The variability between studies of rates of peritoneal dialysis technique failure is attributed, in part, to the lack of a standardized definition of technique failure. The composite recommended definition of peritoneal dialysis technique failure is transfer to hemodialysis therapy for >30 days or death on peritoneal therapy or within 30 days of transfer to hemodialysis therapy. There have been only two studies examining risk factors for early technique failure in peritoneal dialysis and neither study used the recommended definition. Further, only a limited number of patient characteristics were included in the adjusted analyses.

At present, there is no consensus on the key risk factors and risk periods for early technique failure in peritoneal dialysis. Emily J. See, MBBS, and colleagues recently conducted a cohort study designed to analyze factors associated with the development of technique failure in the first year of peritoneal dialysis. The researchers also sought to describe the time-dependent variation in the cause of technique failure. Study results were reported in the American Journal of Kidney Diseases [2018;72(2):188-197].

The multicenter cohort study utilized data from patient records in the Australia and New Zealand Dialysis and Transplant Registry. The registry collects data from all units in Australia and New Zealand on all patients receiving renal replacement therapy (RRT). All adults ≥18 years of age who initiated peritoneal dialysis from January 1, 2000, through December 31, 2014, were included in the study (n=16,748). The cohort included patients who had previously received RRT in the form of hemodialysis or kidney transplantation. Patients were censored at the time of kidney transplantation, recovery of kidney function, loss to follow-up, or 365.25 days after peritoneal dialysis therapy initiation.

Of the 16,748 patients, 726 received a kidney transplant within the first year of peritoneal dialysis therapy, 188 recovered kidney function sufficient to cease dialysis therapy, and 13 were lost to follow-up. Median age of the cohort was 61 years, 58% were male, and 68% were white. There were 4389 (26.2%) patients who experienced technique failure within the first year: 17.8% switched to hemodialysis therapy and 8.4% died. Those with early technique failure were more likely to be >70 years of age; be white; have body mass index (BMI) <18.5 kg/m²; have a history of ischemic heart disease, cerebrovascular disease, or peripheral vascular disease; or be referred late to a nephrology service.

Patients with technique failure were also less likely to be incident to RRT, to receive continuous ambulatory peritoneal dialysis, to have initiated peritoneal dialysis in 2010 through 2014, or to be managed in a larger center or in New Zealand.

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Takeaway Points

- Technique failure in the first year of peritoneal dialysis therapy is associated with increased risk for infection, prolonged hospitalization, mortality, and rising healthcare costs.
- Researchers conducted a multicenter cohort study to examine factors associated with the development of early technique failure and describe time-dependent variation in the cause of technique failure within the first year of peritoneal dialysis.
- Factors associated with increased risk for early technique failure included age >70 years, diabetes or vascular disease prior renal replacement therapy, late referral to nephrology service, or being managed in a smaller center.
- Technique failure is a complex clinical issue and the use of registry data led to a lack of some demographic, clinical, and laboratory variables. There were also no data available on management protocols and training practices in place in individual units, use of disconnect systems, catheter type, and timing between catheter insertion and start of therapy, creating the possibility of residual confounding. Several modifiable and nonmodifiable factors are associated with early technique failure in peritoneal dialysis. Targeted interventions should be considered in high-risk patients to avoid the consequences of an unplanned transfer to hemodialysis therapy or death, the researchers said.
Atrial fibrillation (AF) affects three to six million people in the United States, and nearly 30 million people worldwide. AF is associated with higher risk of mortality and adverse cardiovascular events including stroke. Among patients with end-stage renal disease (ESRD), the prevalence of AF is particularly high compared to the general population. In addition, the 1-year mortality risk of patients with ESRD with AF is two times higher than in those without AF.

Compared with dialysis, kidney transplantation is the treatment of choice for ESRD, improving survival and quality of life for the majority of patients with ESRD. Advances in immunosuppression and in surgical techniques have improved the short-term allograft survival in renal transplant patients; however, long-term allograft survival remains a concern. The incidence and potential consequences of AF may be affected by the improvement of renal function following transplantation; conversely, immunosuppressive agents, insulin resistance, and metabolic syndrome following transplantation may have an impact on those potential consequences.

Charat Thongrayoon, MD, and colleagues recently conducted a meta-analysis designed to summarize available data on (1) the prevalence of pre-existing AF and/or the incidence of post-transplantation AF; (2) outcomes of kidney transplant recipients with AF; and (3) the trends of the estimated incidence of AF after kidney transplantation over time. Results of the meta-analysis were reported online in the Journal of Clinical Medicine [doi:10.3390/jcm7100370].

Risk factors for AF after kidney transplantation included older recipient age, higher body mass index, and a history of coronary artery disease/acute myocardial infarction.

The researchers performed a systematic literature search of MEDLINE (1946 to March 2018), EMBASE (1988 to March 2018), and the Cochrane Database of Systematic Reviews (database inception to March 2018) using a search strategy that combined the terms of “kidney” or “renal” AND “transplant” OR “transplantation” AND “atrial fibrillation.” Eligibility criteria for studies were clinical trials or observational studies (cohort, case-control, or cross-sectional), and reporting the prevalence of pre-existing AF or the incidence of AF after kidney transplantation or outcomes of kidney transplant recipients with AF. Eligible studies had to provide data on prevalence or incidence or effect estimates relative risks, odds ratios (OR), or hazard ratios (HR) with 95% confidence intervals (CI).

The search revealed 399 potentially eligible articles. Following exclusion of 382 articles based on the title and abstract not meeting inclusion criteria, 17 articles underwent full review. Of those, six were excluded due to lack of data on the outcome of interest and three were excluded due to study design, resulting in a final analysis of eight cohort studies representing 137,709 patient-years of follow-up.
kidney transplant recipients. The pooled estimated prevalence of pre-existing AF in patients undergoing kidney transplantation was 7.0% (95% CI, 5.6%-8.8%; I²=86%); the pooled estimated incidence of AF after kidney transplantation was 4.9% (95% CI, 1.7%-13.0%; I²=99%). After limiting the data to new-onset AF after kidney transplantation, the pooled estimated incidence of new-onset AF was 4.2% (95% CI, 1.6%-10.6%; I²=94%).

Results of meta-regression analyses did not show significant correlations between year of study and either prevalence or pre-existing AF or AF following kidney transplantation.

Risk factors for AF after kidney transplantation included older recipient age, higher body mass index, and a history of coronary artery disease/acute myocardial infarction. The pooled OR of mortality among kidney transplant recipients with AF was 1.86 (three studies; 95% CI, 1.03-3.35; I²=98%). Among the population of kidney transplant recipients, AF was associated with death-censored loss of allograft (two studies; OR, 1.55; 95% CI, 1.02-2.53; I²=94%) and stroke (three studies; OR, 2.54; 95% CI, 1.11-5.78; I²=83%).

Limitations to the study cited by the researchers included (1) the presence of statistical heterogeneities, (2) relatively short follow-up periods in the studies analyzed, (3) the inability to determine whether outcomes would be improved with the use of anticoagulation (warfarin and other agents) in kidney transplant recipients, and (4) due to the observational design of the included studies, the meta-analysis could only reveal association rather than a causal-effect relationship between kidney transplantation and AF.

In conclusion, the researchers said, “In spite of progress in transplant medicine, incidence of AF following kidney transplants does not seem to decrease over time. When compared to those without AF, this meta-analysis shows that kidney transplant recipients with AF may carry higher risks of mortality, renal allograft loss, and stroke.”

**TAKEAWAY POINTS**

- Among kidney transplant recipients, those with atrial fibrillation (AF) face a 1-year mortality risk that is twice as high as among those without AF.
- Researchers conducted a systematic review and meta-analysis to examine data on the prevalence of pre-existing AF and/or the incidence of AF after transplantation; outcomes of transplant recipients with AF; and trends in estimated incidence of AF post-transplantation.
- The risks of mortality, renal allograft loss, and stroke appear to be higher among kidney transplant recipients with AF compared with those without AF.
Researchers conducted an analysis of data from one prospective and one retrospective cohort study conducted at multiple transplant centers in Canada and Australia to estimate the time required for donors to complete the evaluation process.

The median total duration of transplantation evaluation was 10.3 months, the median duration from start of the evaluation process to donation was 7.9 months, and from approval to donation was 3.7 months.

Following adjustment, the total duration of transplantation evaluation was longer if the donor participated in paired donation (6.6 months) and if the recipient was referred later relative to the donor’s evaluation start date (0.9 months [per month of delayed referral]). The results depended on whether the recipient was receiving dialysis therapy.

The researchers cited some limitations to the study, including examining data from donors only, the lack of information on program-level factors that may explain variability in donor evaluation times, using proxy dates to estimate some evaluation times, and the possibility that the results may not be generalizable to living donor programs in other countries with different healthcare systems and processes for donor evaluation.

In conclusion, the researchers said, “This study was prompted by a consensus that an evaluation time of 6 months is too long for many donors. The transplantation community needs to further explore and define the reasons why some candidates experience prolonged evaluations and why some transplantation centers have much longer evaluation times than others. Better understanding of these reasons can inform quality improvement initiatives to improve the experiences of candidates going through the evaluation process.”

Coronary Artery Calcification Score in Recipients of Renal Transplant

San Diego—There is an association between coronary artery calcification and cardiovascular morbidity. Due to the heterogeneity in the population of kidney transplant recipients, there may be variation in the presence and severity of coronary artery calcification in these patients.

Using baseline data from a clinical trial, Jennifer S. Lees, MBChB, MRCP, and colleagues in Scotland recently conducted an analysis to identify the factors associated with coronary artery calcification in a population of kidney transplant recipients. Results of the analysis were reported during a poster session at Kidney Week 2018 in a poster titled Factors Associated with Coronary Artery Calcification Score in Renal Transplant Recipients.

Recipients of a kidney transplant participating in a clinical trial of vitamin K supplementation (VITKODIES: ISRCTN22012044) were included in the current analysis. Biochemical tests were conducted and demographic data were collected and recorded at the baseline visit. Non-contrast computed tomography coronary calcium (Agatston) score was used to determine coronary artery calcification. A score >160 was considered high. Factors associated with a high coronary artery calcification score were determined using binary logistic regression analysis. The analyses were conducted using stats and odds ratio (OR) for R statistical software.

The analysis included data on 68 trial participants. Of those, 70.6% were male and 29.4% were female. Compared with participants with lower coronary artery calcification score, those with high coronary artery calcification score [OR 3.88; median score 1269] were older (60.8 years vs. 54.7 years; P = 0.01) with similar systolic blood pressure [152 mm Hg vs. 144 mm Hg; P = 0.08] and proteinuria [urine protein creatinine ratio 98 mg/mmol vs. 72 mg/mmol; P = 0.56], but had longer time since renal transplant (11.2 years vs. 7.4 years; P = 0.05) and time since initial renal replacement therapy (17.0 years vs. 9.8 years; P = 0.02).

There was no difference between the two groups in graft function (glomerular filtration rate, 50.6 mL/min/1.73 m² vs. 53.0 mL/min/1.73 m²) and both groups had controlled calcium phosphate and parathyroid hormone. Both groups also commonly had vitamin D insufficiency (vitamin D <30 ng/mL [71.1% vs. 63.0%; P = 0.54]). Results of binary logistic regression analysis demonstrated that factors associated with high coronary artery calcification score were older age (OR, 1.18 per 10-year increase; 95% confidence interval [CI], 1.05-1.33); longer duration of non-transplant renal replacement therapy (OR, 1.02 per year; 95% CI, 1.01-1.04); and current or previous smoking history (OR, 1.35; 95% CI, 1.09-1.67).

In a diverse group of renal transplant recipients, high coronary artery calcification score was associated with older age, dialysis vintage, and smoking status, but not with traditional markers of chronic kidney disease mineral and bone disorder or vitamin D insufficiency. These offer few modifiable risk factors for intervention, though smoking cessation may be worthwhile. Activity of calcification inhibitors may be important in this patient group and warrant further study,” the researchers said.

RenalytixAI Developing AI-Enabled Clinical Diagnostic Products for Kidney Disease

RenalytixAI, a developer of artificial intelligence-enabled clinical diagnostics for kidney disease, has raised $29 million to support the development and commercialization of two product categories for the early detection of kidney disease and accurate management of kidney transplant rejection. The launch of the first product, KidneyIntelX™, is planned for 2019; the launch will be conducted in collaboration with the Icahn School of Medicine at Mount Sinai, the medical school of the Mount Sinai Health System.

RenalytixAI began trading publicly on AIM, a market of the London Stock Exchange, on November 6, 2018, following the successful completion of the fundraising.

In a press release from RenalytixAI, James McCullough, chief executive officer, said, “RenalytixAI now has the financial resources to drive advanced diagnostic development to improve the management and cost of kidney disease. We are grateful to our investors and medical collaborators who are committed to reducing the impact of this disease.”

Erik Lium, PhD, executive vice president of Mount Sinai Innovation Partners, said, “We’re pleased to be collaborating with RenalytixAI, an emerging industry leader in health AI, on the development of breakthrough prognostics and diagnostics for renal disease. Renal disease represents an increasing healthcare crisis globally, and early detection and intervention can change the course of this disease.”

The technical platform will draw from distinct sources of health data, including systems containing extensive electronic health records, predictive blood-based biomarkers and other genomic data from analysis by high-performance, learning computer algorithms. By combining these inputs, RenalytixAI can create novel models for predicting disease progression and drug/therapy response in individual patients. The company will submit KidneyIntelX to the US Food and Drug Administration for regulatory review.

ClearGuard® HD Caps Reduce Bloodstream Infections

Results from a 2017 study reported in the American Journal of Kidney Diseases demonstrated that ClearGuard® HD Antimicrobial Barrier Caps were superior to standard hemodialysis caps in reducing central line-associated bloodstream infections; patients treated using the ClearGuard caps had an ~70% reduction in central line-associated bloodstream infections compared with standard hemodialysis caps. The study results were highlighted in a recent press release from Pursuit Vascular.

The press release also noted results of a 2018 study, reported in the Journal of the American Society of Nephrology, that compared use of ClearGuard caps to use of Tego® Connector + Curos™ Caps (control group). The findings were similar to those in the earlier study, with 63% to 82% reductions in central line-associated bloodstream infections with use of the ClearGuard cap.

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Dallas, Texas

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News Briefs

Fresenius Medical Care North American Donates Record Funding for Kidney Walk Fundraisers

Fresenius Medical Care North America (FMCNA) has raised more than $800,000 for the Kidney Walk fundraiser sponsored by the National Kidney Foundation, according to a press release from Fresenius Medical Care and the National Kidney Foundation. Kidney Walk is the largest fundraising initiative fighting kidney disease in the United States.

The contribution from Fresenius included a $400,000 corporate donation and more than $400,000 in donations raised by FMCNA employees who participated in the walks. More than 5,600 FMCNA employees joined approximately 400 teams at 71 Kidney Walks across the country.

Bill Valle, chief executive officer of FMCNA, said, “Our partnership with the National Kidney Foundation is one of the ways we live our mission to improve the quality of life of every patient every day. I am humbled by the incredible enthusiasm and support our employees demonstrated throughout the 2018 walks. This is just one of the many examples of how our teams go above and beyond every day to put our patients first.”

Kevin Longino, chief executive officer of the National Kidney Foundation and a kidney transplant recipient, said, “Exceeding this year’s fundraising goal is a big win for everyone affected by kidney disease and we’re proud of our partnership with FMCNA. Since 2012, FMCNA has been on the front lines with us in the fight to raise awareness about and find solutions for kidney disease, and to improve the lives of patients with kidney disease.”

The National Kidney Foundation holds walks in more than 100 communities; 81 cents of every dollar donated goes directly to support National Kidney Foundation programs and services.

Allena Pharmaceuticals Reaches Alignment with FDA on Phase 3 Program for Reloxaliase

Allena Pharmaceuticals has announced that the company has reached alignment with the FDA on the design of a phase 3 trial for reloxaliase in patients with enteric hyperoxaluria as well as an accelerated pathway to pursue a Biologies License Application (BLA) submission for reloxaliase. If approved, reloxaliase could be the first treatment for enteric hyperoxaluria approved by the FDA.

• Investigating a patient’s family history could be a determining factor toward improving outcomes for other relatives.

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He has her eyes.
And maybe her Alport syndrome.

When you see patients with abnormal kidney function, think Alport syndrome. It can filter through the family:

- Alport syndrome is a rare disease and is the second leading cause of inherited chronic kidney disease after polycystic kidney disease.
- Alport syndrome is a progressive, genetic kidney disease that can lead to dialysis, transplant, and/or death.

Abnormal kidney function could be Alport syndrome. It’s time to start making the family connection.

Reata is focused on targeting novel molecular pathways to treat life-threatening diseases that have few or no FDA-approved therapies, including Alport syndrome.

We look forward to working with investigators, clinicians, and patient advocates as we advance reloxaliase as potentially the first therapeutic approved for patients with enteric hyperoxaluria.”

Craig Langman, MD, head of the division of kidney diseases at the Ann & Robert H. Lurie Children’s Hospital, Chicago, said, “Patients with enteric hyperoxaluria suffer from the sudden onset of debilitating kidney stone episodes in addition to the silent deposition of calcium oxalate crystals, both of which can damage the kidney, leading to progressive chronic kidney disease and ultimately end-stage renal disease. Based on the clinical data reported to date, I believe reloxaliase has the potential to offer a critical new therapeutic option to these patients, who currently have no approved pharmacologic interventions.”

Results of Treatment with H.P. Acthar Gel® for Post-Transplant Recipients with FSGS

In a press release, Mallinckrodt announced publication of results of a retrospective analysis assessing the efficacy of H.P. Acthar Gel® in kidney transplant patients with treatment-resistant focal segmental glomerular sclerosis (FSGS). Analysis results were reported in Transplantation. The analysis included data from patients treated at two large US transplant centers between April 2012 and December 2016.

The study evaluated 20 kidney transplant recipients (mean age, 49 years) who received H.P. Acthar Gel for the treatment of proteinuria due to new or recurrent post-transplant FSGS. The analysis found significant improvement in proteinuria following treatment; 50% of patients who received the gel had a complete or partial remission of proteinuria.
Results of a study designed to identify and test whether acute kidney injury (AKI) subphenotypes have prognostic and therapeutic implications were reported by Pavan K. Bhatraju, MD, and colleagues. Latent class analysis methodology was applied independently in two critically ill populations (discovery, n=794, and replication, n=425) with AKI. AKI subphenotypes were identified using a parsimonious classification model. The model was then applied to patients with AKI in the VASST (Vasopressin in Septic Shock) trial (n=271) to determine differences in treatment response. AKI was defined using serum creatinine and urine output in all three populations.

In both the discovery and replication AKI groups, the best fit was a two-subphenotype LCA model (P<.004 in both groups). Relative to AKI subphenotype 1 (AKI-SP1), the risk of 7-day renal non-recovery and 28-day mortality was greater with AKI subphenotype 2 (AKI-SP2). The AKI subphenotypes discriminated risk for poor clinical outcomes better than the Kidney Disease Improving Global Outcomes AKI stages. A three-variable model that included markers of endothelial dysfunction and inflammation accurately determined subphenotype membership.

In VASST, vasopressin compared with norepinephrine was associated with improved 90-day mortality in AKI-SP1 (27% vs 46%; respectively; P=.02); there was no significant difference in AKI-SP2 (45% vs 49%, respectively; P=.99).

In conclusion, the researchers said, “This analysis identified two molecularly distinct AKI subphenotypes with different clinical outcomes and response to vasopressin therapy. Identification of AKI subphenotypes could improve risk prognostication and may be useful for predictive enrichment in clinical trials.”

**Outcomes of Early AKI after Heart Transplantation**

Transplantation. 2018;102(11):1901-1908

There are few data available regarding the incidence of acute kidney injury (AKI) (defined using the Kidney Disease Improving Global Outcomes classification) after heart transplantation. Renata Garcia-Gigorro, MD, PhD, recently conducted a study designed to assess the impact of AKI in a cohort of heart transplant recipients.

The study included 310 consecutive heart transplant recipients from 1999 to 2017. Risk factors were examined using multivariable analyses; survival was assessed by Kaplan-Meier curves and a risk-adjusted Cox proportional hazards regression model.

Of the total cohort, 40.3% (n=125) of patients developed AKI, 23.5% (n=73) of those had AKI stage 1, 5.8% (n=18) had AKI stage 2, and 11% (n=34) had AKI stage 3. The principal risk factors for AKI were cardiac tamponade (odds ratio [OR], 16.82; 95% confidence interval [CI], 1.06-138), acute right ventricular failure (OR, 3.54; 95% CI, 1.82-6.88), and major bleeding (OR, 2.46; 95% CI, 1.18-5.1).

Patients with AKI had greater hospital mortality than those without AKI (3.8% vs 16%; P=.05); the risk was greatest among patients who required renal replacement therapy (RRT) (46.9% vs 5.4%; P=.006). There was an independent association between AKI requiring RRT and hospital mortality (OR, 11.03; 95% CI, 4.08-29.8).

With median follow-up following hospital discharge of 6.7 years, overall survival among patients without AKI at 1, 5, and 10 years was 95.4%, 85.1%, and 75.4%, respectively, compared with 85.2%, 69.8%, and 63.3%, respectively, among patients with AKI stages 2 to 3 (P=.08).

In conclusion, the researchers said, “The onset of AKI after heart transplantation is mainly associated with postoperative complications. Only severe AKI stage predicts worse short-term outcome, with this impact appearing to be lost at long-term follow-up.”

**DIALYSIS**

**Intensive Glycemia Control May Result in Reduction in Macroalbuminuria**

Clinical Journal of the American Society of Nephrology. doi.org/10.2215/CJN.06200518

Studies of short-term (<5 years) kidney outcomes among people with type 2 diabetes treated with interventions to maintain aggressive control of glycemia, blood pressure, and lipids have shown conflicting results. Amy K. Mottl, MD, MPH, and colleagues recently conducted a post hoc analysis aimed at determining the long-term renal effects of such interventions. The analysis utilized data from the ACCORD (Action to Control Cardiovascular Risk in Diabetes) trial and ACCORDIAN, the ACCORD follow-on study.

The post hoc primary composite kidney outcome was defined as incident macroalbuminuria, creatinine doubling, need for dialysis, or death by any cause. The effect of each intervention on the composite outcome and individual components was estimated using Cox proportional hazards regression. In secondary outcome analyses, competing risk regression was used to account for the risk of death in incident kidney outcomes. The analyses were adjusted for sociodemographic, randomization groups, and clinical factors.

**DIALYSIS**

Provision of Peritoneal Dialysis Following Prospective Payment System Implementation

Clinical Journal of the American Society of Nephrology. 2018;13(12):1833-1841

Compared with hemodialysis, peritoneal dialysis is associated with equivalent mortality, higher quality of life, and lower costs. In 2011, the Centers for Medicare & Medicaid services implemented a comprehensive prospective payment system that makes a single payment for all dialysis, medication, and ancillary services. Researchers, led by Virginia Wang, PhD, conducted a longitudinal retrospective cohort study designed to assess whether the prospective payment system increased dialysis facility provision of peritoneal dialysis and whether changes in peritoneal dialysis provision were more common in dialysis facilities that are chain affiliated, and located in nonurban areas and in regions with high dialysis market competition.

The study included 6433 nonfederal dialysis facilities in the United States before and after implementation of the prospective payment system (2006-2010 and 2011-2013, respectively). The researchers utilized data from the US Renal Data System, Medicare, and Area Health Resource Files. The outcomes of interest were a dichotomous indicator of peritoneal dialysis availability and a discrete count variable of dialysis facility peritoneal dialysis program size, defined as the annual number of patients receiving peritoneal dialysis service offerings, peritoneal dialysis program size, and whether changes differed by chain affiliation, urban location, facility size, or market competition.
Following implementation of the prospective payment system, there was a modest increase in observed facility provision of peritoneal dialysis and in peritoneal dialysis program size (36% and 5.7 patients in 2006 to 42% and 6.9 patients in 2013, respectively. There was a positive association between implementation of the prospective payment system and provision of peritoneal dialysis (odds ratio [OR], 1.20; 95% confidence interval [CI], 1.13-1.18) and peritoneal program size (incidence rate ratio, 1.27; 95% CI, 1.22-1.33).

The change in provision of peritoneal dialysis following prospective payment system use was greater among nonurban, chain-affiliated, and larger-sized facilities (P<.001, P=.002, and P<.001, respectively). There were higher rates of peritoneal dialysis program size growth in nonurban facilities following implementation of the prospective payment system (P<.001).

In conclusion, the researchers said, “Medicare’s 2011 prospective payment system was associated with more facilities’ availability of peritoneal dialysis and modest growth in facility peritoneal dialysis program size.”

END-STAGE RENAL DISEASE

Health Risks after Incident Atrial Fibrillation in Patients on Hemodialysis

Nephrology Dialysis Transplantation. 2018;33(9):1590–1597

There are limited data on the cardiovascular risks of incident atrial fibrillation/flutter (AF) in patients with end-stage renal disease (ESRD) undergoing hemodialysis. Medha Airy, MD, and colleagues conducted a study of older patients in the United States who initiated hemodialysis for ESRD from 2006 to 2011 who had not been previously diagnosed with AF, stroke, myocardial infarction (MI), or hip fracture. To estimate hazard ratios (HRs) for the events of ischemic stroke, MI, and death, the researchers used Cox regression with AF as a time-varying covariate, adjusted for sociodemographic characteristics and comorbidities. Hip fracture was used as a negative control outcome.

The researchers identified 85,377 older patients (mean age, 76.5 years) who initiated hemodialysis for ESRF from 2006 to 2011 who had not been previously diagnosed with AF, stroke, myocardial infarction (MI), or hip fracture. To estimate hazard ratios (HRs) for the events of ischemic stroke, MI, and death, the researchers used Cox regression with AF as a time-varying covariate, adjusted for sociodemographic characteristics and comorbidities. Hip fracture was used as a negative control outcome.

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In conclusion, the researchers said, “Follow-up for up to 11.2 years (average 4.6 years) showed a sustained reduction in the annual rate of eGFR decline in patients treated with tolvaptan compared with controls and an increasing separation of eGFR values over time between the two groups.”

POLYCYSTIC KIDNEY DISEASE

Long-Term Treatment with Tolvaptan for ADPKD Safe and Effective


In the TEMPO (Tolvaptan Efficacy and Safety in Management of ADPKD and Its Outcomes) 3:4 and the REPRISE (Replicating Evidence of Preserved Renal Function: An Investigation of Tolvaptan Safety and Efficacy in ADPKD) trials, patients with autosomal dominant polycystic kidney disease (ADPKD) had decline in estimated glomerular filtration rate (eGFR) at early and later stages, respectively. Marie E. Edwards and colleagues conducted an analysis to determine whether the reduction in eGFR associated with tolvaptan is sustained, cumulative, and likely to delay the need for renal replacement therapy in that patient population.

In all, 128 patients with ADPKD participated in the clinical trials of tolvaptan at the Mayo Clinic. All of the 128 patients had the opportunity to participate in the open-label extension studies; 20 participated in short-term studies or received placebo only. The remaining 108 were analyzed for safety. Three approaches were used to evaluate 97 patients treated with tolvaptan for 21 years: (1) comparison of eGFR slopes and outcome (33% reduction from baseline eGFR to controls matched by sex, age, and baseline eGFR; (2) stability of eGFR slopes with duration of follow-up; and (3) comparison of observed and predicted eGFRs at last follow-up.

Comparing with controls, patients treated with tolvaptan had lower eGFR slopes from baseline and from month 1, as well as lower risk of a 33% reduction in eGFR. There was no change in annualized eGFR slopes of patients treated with tolvaptan during follow-up; differences between observed and predicted eGFRs at last follow-up increased with duration of treatment.

In conclusion, the researchers said, “Long-term treatment with tolvaptan was also an association between incident AF and higher adjusted risk of ischemic stroke: 2.1 during the first 30 days, 2.5 between 31 and 90 days, and 1.5 beyond 90 days. Findings for MI were similar. The risk of hip fracture was only marginally increased following a diagnosis of AF. When incident AF was defined by a primary diagnosis code, all associations were attenuated and the association with hip fracture was null.

“AF was strongly associated with increased risks of ischemic stroke, MI, and death, with risks highest soon after AF diagnosis but extending beyond 90 days,” the researchers said.

In recipients of kidney transplantation, treatment with everolimus permits reduced calcineurin inhibitor (CNI) exposure; however, the efficacy and safety outcomes in that patient population are unclear.

Julio Pascual, MD, PhD, and colleagues conducted a multicenter noninferiority trial that included 2038 de novo kidney transplant recipients. The participants received, in combination with induction therapy and corticosteroids, either everolimus with reduced-exposure CNI (everolimus arm, n=1022) or mycophenolic acid (MPA) with standard-exposure CNI (MPA arm, n=1015). The primary end point was treated biopsy-proven acute rejection or estimated glomerular filtration rate <90 mL/min/1.73 m2 at 12 months post-transplant using a 10% noninferiority margin.

In the overall cohort, the incidence of the primary end point was 48.2% (n=493) in the everolimus arm and 45.1% (n=467) in the MPA arm (difference, 3.2%; 95% confidence interval [CI], 1.3% to 7.6%). In subgroups of patients who received tacrolimus or cyclosporine, the differences in incidence between the two arms were similar.

In the everolimus arm, treated biopsy-proven acute rejection, graft loss, or death at 12 months post-transplant occurred in 14.9% of patients; in the MPA arm, the incidence was 12.8% (difference, 2.3%; 95% CI, 1.3% to 7.2%). There was no difference between the two arms in de novo donor-specific antibody incidence at 12 months post-transplant or in the antibody-mediated rejection rate.

Cytomegalovirus and BK virus infections were less common in the everolimus arm compared with the MPA arm (3.6% vs 13.5% and 4.3% vs 8.0%, respectively). In all, 23.0% of patients in the everolimus arm and 11.9% of patients in the MPA arm discontinued the study drug due to adverse events.

In conclusion, the researchers said, “In kidney transplant recipients at mid-to-moderate immunologic risk, everolimus was noninferior to MPA for a binary composite end point assessing immunosuppressive efficacy and preservation of graft function.”
Patient Payments Part Two

Last issue I mentioned that a social worker commented to me that she wished providers would stop trying to collect from patients. She said providers “make enough money” and wondered why they feel the need to collect from patients who cannot afford their large co-insurances and deductibles. She pointed out that increasing pressure on patients to pay for co-insurances and deductibles for renal services can cause them to discontinue needed treatments. While providers might appear to be the bad guys for trying to collect from patients, there were three major changes over the past 11 years that put great pressure on providers to pursue payments from patients. The changes consisted of plummeting reimbursement, significant changes in government regulations, and public ownership of renal companies. Lower reimbursement in the last issue so this month’s column will focus on the remaining issues.

MEDICARE BAD DEBT

While several government policies have influenced renal providers to apply greater pressure on patients for payment, the primary culprit from my perspective was the change in Medicare Bad Debt regulations in the latter portion of 2007. Prior to the change, a dialysis facility was required to bill patients for unpaid Medicare deductibles and co-insurances, but if patients did not pay, the facility was not required to press the patients for payment. If sending bills did not result in full payment, facilities could claim the unpaid amounts on their annual cost report as bad debt. Up to 100% of the amount claimed would be reimbursed to the provider by Medicare.

In an effort to curb Medicare costs, providers were required to make more than a “token collection effort” to collect out-of-pocket amounts from patients. Under the revised regulations, in addition to billing the patient, providers were required to take “other actions such as subsequent billings, collection letters and telephone calls or personal contacts...which constitute a genuine...collection effort.” (CMS PBM 151.05)

Medicare contractors began earnestly enforcing these requirements beginning with the 2007 and 2008 cost reports. Millions of dollars in bad debt that would have been reimbursed under the old regulations were now lost to dialysis providers. Even with the loss of reimbursement, most providers remained extremely reluctant to pressure patients for payment. However, the federal government also decided to reduce their reimbursement for qualifying bad debt from 100% to 65%. Thus, even the bad debts that still qualified under the new regulations were reduced by approximately one-third. Coupled with declining reimbursement from commercial and other government payers, facility owners eventually decided they would have to comply with the revised bad debt regulation and apply more pressure on patients to pay for their unpaid Medicare co-insurance and deductible.

Without exception, dialysis providers were extremely concerned about how their patients would respond to the increased pressure to pay. No one in the ESRD industry wanted a patient to stop dialyzing because they felt pressure to pay more out of their own pockets. To minimize patients’ distress, many independent facilities assigned their social workers to speak with patients about paying for out-of-pocket liabilities. However, social workers understandably balked at such an assignment and eventually most facilities decided to place the burden of collection on those in their back office. Small facilities without a back office had to rely on a secretary, receptionist, or administrator to try and collect from patients. Of course, this was also awkward and, over time, the burden and discomfort of confronting ESRD patients about money resulted in many programs outsourcing their collection efforts. Most providers instructed collection agencies to take a soft approach with their patients to minimize patient distress. Nevertheless, their patients were now receiving calls from collection agencies about paying for out-of-pocket costs, primarily for the sake of satisfying the requirements of Medicare’s bad debt regulation.

Does anyone see anything wrong with this picture? Prior to the change in bad debt requirements, ESRD providers were willing to forgo pressuring patients for money. In an effort to reduce the Medicare budget, well intentioned laws and regulations were enacted that put significant financial pressure on ESRD providers to go after their patients for money. Most dialysis patients are older, unable to work, and financially challenged. Yet they are expected to pay tremendous amounts out of pocket each month. Those who can afford secondary insurance policies receive some relief, but skyrocketing annual deductibles have resulted in patients having to pay out of pocket for their co-insurance for much of the year.

While I understand the need for those who receive Medicare coverage to pay something for the benefit they receive, it seems that ESRD patients have an undue burden placed upon them by being required to pay the same 20% co-insurance as those without a chronic disease. However, rather than policies that decrease their burden, these fragile patients face increased pressure from their own providers to pay for the life-saving services they receive. Providers look like the “bad guys,” but most patients and clinical workers are unaware of the policies that have resulted in our current situation.

PUBLIC OWNERSHIP

Publicly owned for-profit companies are responsible to their shareholders for their bottom line. Shareholders demand positive returns on their investments. Thus, these companies have an additional pressure to pursue out-of-pocket payments from patients in order to garner every penny they can. However, could shareholders agree to take a penny or two less in order to not pursue ESRD patients for payments that are small to the corporation, but huge for patients? Could our government not decrease the percentage of the Medicare co-insurance assigned to ESRD patients? And why not revise the bad debt regulations for ESRD so that providers will not feel so much pressure to pursue money from their patients?

Rick Collins is the director of business development for Sceptre Management Solutions, a company specializing in billing for outpatient ESRD facilities, nephrology practices, and vascular access. Your questions and comments are welcome and he can be reached at rcollins@sceptremanagement.com or 801.775.8010.
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