The New Kidney Allocation System

By Udey S. Nori

Ever since deceased donor kidney transplantation became practical and accessible to all, several competing factors have shaped the kidney allocation system (KAS) in the US. On one hand, scientific progress has allowed vastly improved preservation techniques, and cross-matching has made it possible to increase the allograft half-life significantly. On the other hand, there continues to be a moral obligation to achieve equity and fairness in organ allocation practices.

Over the past several years, other issues have become increasingly important: the demand for deceased donor kidneys continues to increase as the supply remains at a plateau, the organ discard rate remains unacceptably high, and more already-treated patients are returning to the list for repeat transplantation. Furthermore, very highly sensitized patients (with preformed anti-HLA antibodies) are harder to match and tend to have very much longer waiting times. Over the past two decades, several minor changes were made to the KAS (e.g., removing HLA-B antigen matching in the match run) to address these issues, but the most significant new KAS was implemented by the Organ Procurement and Transplantation Network/United Network of Organ sharing (OPTN/UNOS) in December 2014.

The overarching goals for the new KAS are as follows:

- Increase the life-years gained from each organ by matching donors and recipients on the basis of their health risk profiles. This is made possible by assigning an estimated posttransplant survival (EPTS) score to a recipient and matching it to the kidney donor profile index (KDPI) of the donor (Tables 1 and 2). This allows allocation of the best quality kidneys to the recipients with the highest predicted longevity.
- Increase the chance for transplantation for highly sensitized patients (highly calculated panel reactive antibodies [CPRA]). This is made possible by expanding the geographic area for organ sharing, allowing these patients to have access to more potential donors.
- Improve procurement of organs from extended criteria donors that could potentially be used for patients with high (suboptimal) EPTS.
- Decrease the organ discard rate of kidneys that were not used despite being procured for transplantation.
- Standardize the waiting times: Patients with delays in the match run to have their waiting time defined as age difference between the donor and the recipient of more than 15 years, has decreased from 50 percent to 48 percent, as did the the proportion of high KDPI transplants to low EPTS candidates (3 percent to 1 percent).
- A few unexpected trends to watch were also noted:
  - A significant drop in the zero-mismatch transplants from 8 percent to 4.5 percent, probably because of the increased priority given to high CPRA patients
  - A higher organ discard rate of 20.3 percent compared to the pre-KAS era rate of 13.5 percent.

The Estimated Posttransplant Survival (EPTS) score

The EPTS is calculated from the following recipient characteristic:
- Age
- Number of years receiving dialysis
- Diabetes mellitus
- Prior kidney transplantation

The Kidney Donor Profile Index (KDPI)

The KDPI is calculated from the following donor characteristics:
- Age
- Height
- Weight
- Ethnicity
- History of hypertension
- History of diabetes
- Cause of death
- Serum creatinine
- Hepatitis C virus status
- Donation after circulatory death status

SGLT-2 Inhibitors: What the Nephrologist Needs to Know

By Andrew J. King, MD

On the lookout for increased use of SGLT-2 inhibitors in 2016 after a recent study published in the New England Journal of Medicine demonstrated a lower composite rate of death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke in high-risk type 2 diabetics (n = 7020) treated with empagliflozin compared to placebo. Reduction in death in the treated group was mostly due to a reduction in cardiovascular deaths (18% risk reduction). Active treatment also reduced renal events by 21% primarily related to a reduction in the development of microalbuminuria.

Empagliflozin is one of several SGLT-2 inhibitors now on the market. This class of drugs represents selective inhibitors of sodium glucose cotransporter 2 in the proximal tubule that lead to substantial glycosuria and hence, a reduction in blood glucose. Patients treated with these agents can have small decreases in weight (typically 2–4 kg) and systolic blood pressure (BP) (4–6 mm Hg), likely related to the osmotic diuresis that accompanies the glycosuria. The major side effect appears to be an increase in urinary tract and genital infections, some leading to septicemia and hospitalization. Ketoacidosis is another unusual complication typically seen within the first year and associated with another risk factor, e.g., fasting, alcohol, or reduction/discontinuation of insulin.

The hypoglycemic effects of SGLT-2 inhibitors diminish with worsening kidney function. SGLT-2 inhibitors are currently not indicated in patients with GFR <30 mL/min. A study using canagliflozin demonstrated hypoglycemic efficacy in CKD stage 3 with small reductions in HbA1c seen within 3 weeks of initiation of drug and a reduction in urinary albumin excretion (20–30% vs. 7.5% in controls). Others have found similar effects on HbA1c, BP, microalbuminuria, and progression of albuminuria. A small study of patients with type 1 diabetes demonstrated a reduction in glomerular hypertrophy by empagliflozin under both euglycemic and hyperglycemic clamped conditions. The authors postulated that the SGLT-2 inhibitor restores tubular-glomerular feedback, leading to an increase in arterial tone.

Taken together, these findings raise the intriguing possibility that early use of SGLT-2 inhibitors might have significant renal protective effects. Does one believe a reduction in proteinuria signals renal protection? Only time and well conducted clinical trials will answer this question as it relates to SGLT-2 inhibitors. However, kidney care givers should prepare to answer questions about the safety and efficacy of SGLT-2 inhibitors, their effects on the kidney, and how they perform in patients with various degrees of renal dysfunction.