

Kidney News

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Does Living Donor Age Matter in Kidney Transplantation?

Recent study results should encourage more donor paired exchanges

By Tracy Hampton



Across the globe, numerous kidney transplant candidates and donors are linking up in often complicated ways to facilitate more transplants through exchange programs, or swaps. The largest swap so far, which was orchestrated by the National Kidney Registry (NKR) and involved 60 lives and 30 kidneys, was described recently in *The New York Times* (http://www.nytimes.com/2012/02/19/health/lives-forever-linked-through-kidney-transplant-chain-124.html?_r=2). Also, in early February the NKR announced that it had facilitated its 400th exchange transplant. These efforts by the NKR and other programs could not come at a better time. Nearly 90,000 people in the United States are waiting for a kidney transplant, and

many will die before a suitable organ becomes available. The shortage is expected to worsen.

Such living donor chains and simpler closed-loop paired exchanges, which involve two pairs of donors and recipients, assume that kidneys from living donors are of comparable quality and anticipated longevity. But how true is this assumption? Potential recipients often wonder, will the kidney received from a stranger—particularly an older one—be as good as a kidney donated by a loved one?

“In a proposed kidney paired donation match, if an old donor–recipient pair is matched to a young donor–recipient pair, the young recipient may feel disadvantaged and may not be will-

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Antiplatelet Therapy in Patients with Chronic Kidney Disease: Is It Safe?

By Tracy Hampton

Antiplatelet therapy that inhibits blood clotting can be life-saving for individuals at high risk for cardiovascular disease or stroke. At first glance, this should apply to patients with chronic kidney disease (CKD), who are more likely to die of cardiovascular disease than of any other cause.

But nonatherosclerotic conditions such as cardiac failure, sudden cardiac death, and arrhythmia are more common causes of cardiovascular events in individuals with CKD than in the general population, and the bleeding risk of antiplatelet agents may be greater among people with CKD because of

impaired hemostasis.

Investigators recently published a review in the *Annals of Internal Medicine* on the benefits and harms of antiplatelet agents in these patients, focusing on cardiovascular events, mortality, and bleeding.

“Until now, data from studies done in the general population were extrapolated to people with chronic kidney disease,” said senior author Giovanni Strippoli, MD, PhD, who holds titles at the school of public health at the University of Sydney in Australia, the Mario Negri Sud Consortium in Italy,

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Antiplatelet Therapy

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and Diaverum in Sweden. “Previous research from our group and others has shown that such extrapolations could be very dangerous, and interventions that may be very good in the general population may have no effect or even be harmful in people with chronic kidney disease

Paying particular attention to patients with CKD while conducting clinical trials will only become more important. Approximately 10 percent to 15 percent of the adult population worldwide have the disease, and its prevalence is on the rise because of increasing rates of diabetes and obesity.

Analyzing available data

Mining Embase and Cochrane databases from 1980 through November 2011 without language restriction, Strippoli and his colleagues selected randomized trials that included adults with CKD and compared antiplatelet agents with standard care, placebo, or no treatment.

“Nephrology is lagging behind all other disciplines of internal medicine when it comes to randomized trials, and a strong effort is needed to do more trials and to summarize existing knowledge from the few small existing trials that have been published,” said Strippoli. Many of the trials in the analysis were not performed to study issues specifically in kidney disease but included a small portion of people with the condition.

Nine trials (9969 participants) provided information on antiplatelet treatment among persons with CKD who had acute coronary syndrome or were undergoing coronary artery intervention and were considered at high risk for subsequent vessel closure. All data for these trials were post hoc analyses for subgroups of participants with CKD from larger trials. The trials provided data for glycoprotein IIb/IIIa inhibitors (abciximab, eptifibatide, or tirofiban) or clopidogrel (two trials, 4498 participants), and all involved coadministration of aspirin with or without heparin. The median follow-up time was 12 months.

Another 31 trials provided data on 11,701 persons with stable or no cardiovascular disease who received antiplatelet therapy. Twelve trials studied antiplatelet effects on mortality, progression of kidney disease, or safety in patients who had glomerulonephritis, diabetic nephropathy, or an impaired GFR regardless of cause. The agents administered included aspirin, dipyridamole, aspirin and dipyridamole, or a thienopyridine (clopidogrel or ticlopidine), and the median follow-up time was 12 months. Seventeen of the trials provided shorter-term data (median of 6 months of follow-up) for a variety of antiplatelet treatments in persons who were receiving or would soon require dialysis. Four trials administered antiplatelet therapy to kidney transplant recipients.

Pros and cons of anticlotting drugs

In general, the investigators found that the available information on antiplatelet therapy in patients with CKD is of low or very low quality, with considerable variation in trial duration, heterogeneity in the definitions and assessment of bleeding outcomes, reliance on subgroup data from major trials, and substantial methodologic limitations in data for patients with stable cardiovascular disease.

The researchers reported low-quality evidence that in people with acute coronary syndromes, glycoprotein IIb/IIIa inhibitors or clopidogrel plus standard care had little or no effect compared with standard care alone on all-cause or cardiovascular mortality or on myocardial infarction, but the treatments increased serious bleeding by up to 40 percent. Also according to generally low-quality evidence, antiplatelet therapy prevented myocardial infarction (lowering the risk by about 34 percent) but caused uncertain effects on mortality and increased minor bleeding by approximately 70 percent compared with placebo or no treatment in persons with stable or no cardiovascular disease.

These findings indicate that any benefits of antiplatelet therapy for people with CKD are uncertain and are potentially outweighed by bleeding hazards.

“All in all, these drugs should be used with care and attention, as all doctors do, and we should always think before we prescribe,” said Strippoli. Also, he and his coauthors noted that many patients would not be likely to accept the risk for major bleeding to reduce their risk for myocardial infarction without proven reductions in death or the need for coronary revascularization.

“This systematic review and meta-analyses primarily highlight the rather limited evidence from existing randomized trials about the efficacy and safety of antiplatelet agents for preventing cardiovascular events and death across the spectrum of chronic kidney disease and in those receiving dialysis or a renal transplant,” said Alan Go, MD, who is the director of the comprehensive clinical research unit and the regional medical director for clinical trials at Kaiser Permanente Northern California and who was not involved with the research.

Given the low quality of the available evidence, the investigators advocate for specific trials evaluating antiplatelet therapies, including newer agents, in individuals with CKD and coexisting acute or stable cardiovascular disease. They also note that no data are currently available on antiplatelet use in dialysis patients or kidney transplant recipients who have acute coronary syndromes or require coronary artery revascularization.

“Given the risks of bleeding associated with these agents, additional studies are needed to delineate the net clinical benefit or harm at different levels of renal function through randomized trials as well as studies done in large, diverse clinical practice populations that are more representative,” said Go. ●