by setting included ESA use, prescriber specialty, and dosage regimen. Results: The most common hospital locations of ESA administration were a cancer center in the outpatient setting (49%) and general medicine (57%) in the inpatient setting. ESA prescribers were most commonly hematologists and oncologists in the outpatient setting, and nephrologists were the most common prescribers in the inpatient setting. In the outpatient analysis, 2155 patients were prescribed darbepoetin alfa and 3106 were prescribed epoetin alfa. The predominant administration frequencies were every two weeks and once weekly for darbepoetin alfa, and once weekly for epoetin alfa. In the inpatient analysis, 1633 patients were prescribed darbepoetin alfa and 3231 were prescribed epoetin alfa. The predominant administration frequencies were once weekly for darbepoetin alfa and once weekly and three times weekly for epoetin alfa. Common uses for both ESAs were chemotherapy-induced anemia (outpatient setting) and anemia of end-stage renal disease with chronic dialysis (inpatient setting). There was considerable variability in ESA dosages and administration frequencies in both settings within all patient groups when analyzed by specified use. Conclusion: ESA use differed between outpatient and inpatient settings in indication, frequency of administration, and specialty of the prescriber.

Editorial Comment: Use of ESAs in Medicare cases has been a contentious issue during the last 2 years. In response to a black box warning regarding these agents the Centers for Medicare and Medicaid Services issued a national coverage determination that restricts their use. Our colleagues in the American Society of Clinical Oncology were among the most vocal opponents of this national coverage determination. Data from this study help us to understand why. In the outpatient setting the most common providers to prescribe these agents were hematologists and oncologists. Obviously there are economic and medical factors driving the differences in use between the inpatient and outpatient settings. As urologists, we need to be aware of these factors for 2 reasons—some urologists use these agents before radical prostatectomy and, more importantly, the Centers for Medicare and Medicaid Services are going to be keeping a closer eye on medication use, particularly with regard to costly agents, in the future.

David F. Penson, M.D., M.P.H.

Renal Transplantation and Renovascular Hypertension

Machine Perfusion or Cold Storage in Deceased-Donor Kidney Transplantation


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Background: Static cold storage is generally used to preserve kidney allografts from deceased donors. Hypothermic machine perfusion may improve outcomes after transplantation, but few sufficiently powered prospective studies have addressed this possibility. Methods: In this international randomized, controlled trial, we randomly assigned one kidney from 336 consecutive deceased donors to machine perfusion and the other to cold storage. All 672 recipients were followed for 1 year. The primary end point was delayed graft function (requiring dialysis in the first week after transplantation). Secondary end points were the duration of delayed graft function, delayed graft function defined by the rate of the decrease in the serum creatinine level, primary nonfunction, the serum creatinine level and clearance, acute rejection, toxicity of the calcineurin inhibitor, the length of hospital stay, and allograft and patient survival. Results: Machine perfusion significantly reduced the risk of delayed graft function. Delayed graft function developed in 70 patients in the machine-perfusion group versus 89 in the cold-storage group (adjusted odds ratio, 0.57; P = 0.01). Machine perfusion also significantly improved the rate of the decrease in the serum creatinine level and reduced the duration
of delayed graft function. Machine perfusion was associated with lower serum creatinine levels during the first 2 weeks after transplantation and a reduced risk of graft failure (hazard ratio, 0.52; P=0.03). One-year allograft survival was superior in the machine-perfusion group (94% vs. 90%, P=0.04). No significant differences were observed for the other secondary end points. No serious adverse events were directly attributable to machine perfusion. Conclusions: Hypothermic machine perfusion was associated with a reduced risk of delayed graft function and improved graft survival in the first year after transplantation.

**Editorial Comment:** Pulsatile perfusion (PP) as a mode of preservation has seen a resurgence recently. The benefits of PP are best illustrated in the improved use and performance of expanded criteria donor kidneys. This finding is important because these types of kidneys are becoming a higher proportion of the usable kidney pool. In addition to obtaining information on viability, PP has been associated with decreased rates of delayed graft function (DGF). This result leads to improved outcomes and lower costs of transplantation.

This well crafted, multicenter study assesses PP by randomizing 1 kidney from each deceased donor pair to undergo PP and the other to standard cold storage preservation. Donors were not selected on the basis of fulfilling expanded donor criteria. The main findings were that machine perfusion was associated with reduced DGF, lower primary nonfunction and improved 1-year graft survival compared to cold storage. Selective performance of machine perfusion in high risk for DGF donor kidneys is increasingly common. This article suggests that even in an unselected group of deceased donor kidneys the benefits are apparent.

David A. Goldfarb, M.D.

**Long-Term Consequences of Kidney Donation**


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Background: The long-term renal consequences of kidney donation by a living donor are attracting increased appropriate interest. The overall evidence suggests that living kidney donors have survival similar to that of nondonors and that their risk of end-stage renal disease (ESRD) is not increased. Previous studies have included relatively small numbers of donors and a brief follow-up period. Methods: We ascertained the vital status and lifetime risk of ESRD in 3698 kidney donors who donated kidneys during the period from 1963 through 2007; from 2003 through 2007, we also measured the glomerular filtration rate (GFR) and urinary albumin excretion and assessed the prevalence of hypertension, general health status, and quality of life in 255 donors. Results: The survival of kidney donors was similar to that of controls who were matched for age, sex, and race or ethnic group. ESRD developed in 11 donors, a rate of 180 cases per million persons per year, as compared with a rate of 268 per million per year in the general population. At a mean (+/−SD) of 12.2+/−9.2 years after donation, 85.5% of the subgroup of 255 donors had a GFR of 60 ml per minute per 1.73 m² of body-surface area or higher, 32.1% had hypertension, and 12.7% had albuminuria. Older age and higher body-mass index, but not a longer time since donation, were associated with both a GFR that was lower than 60 ml per minute per 1.73 m² and hypertension. A longer time since donation, however, was independently associated with albuminuria. Most donors had quality-of-life scores that were better than population norms, and the prevalence of coexisting conditions was similar to that among controls from the National Health and Nutrition Examination Survey (NHANES) who were matched for age, sex, race or ethnic group, and body-mass index. Conclusions: Survival and the risk of ESRD in carefully screened kidney donors appear to be similar to those in the general population. Most donors who were studied had a preserved GFR, normal albumin excretion, and an excellent quality of life.
Editorial Comment: The long and short-term safety of kidney donation remains an important issue in transplantation. This article is a comprehensive look at the longer term outcomes of living donors from a single center with more than 4 decades of experience. The authors examined vital statistics of the overall group. Extended evaluation of renal function by iohexol studies, albuminuria assessment, blood pressure measurements and quality of life assessment were performed in representative samples of donors (255) based on time from donation and gender. Vital statistics show that donors have a life expectancy similar to the general population.

ESRD developed in 11 donors, yielding an incidence of 180 per million persons annually, compared to 268 per million persons annually for the white population of the United States. GFR was well preserved and actually increased with longer followup. The risk of low GFR (less than 60 ml per minute) was associated with age, body mass index and female sex. Albuminuria was associated with time from donation. Hypertension was associated with advancing age and body mass index. Compared to a NHANES control group, donors had improved lipid profiles and lower rates of cancer.

These data add to the compendium of long-term kidney donor outcomes. This information provides testimony to the safety of donation given the selection criteria outlined by the study. These findings are important to discuss with candidates considering renal donation.

David A. Goldfarb, M.D.