Grace *et al.*'s analysis, the profile of LKD relationships and the reduced chance of receiving an LKD transplant associated with socioeconomic status remained constant between states and across time despite marked differences between states and increases over time in absolute LKD rates. Perhaps one reason for this is the relatively low percentage of patients in Australia who are activated on the transplant waiting list compared with other countries—18% of dialysis patients younger than 65 in Australia compared with 49% in France, 48% in the United Kingdom, and 33% in the United States.[8]

There are also some noteworthy high-achieving transplant program models around the world. In Norway, a very active LKD program makes it possible for nearly 90% of patients younger than 65 on dialysis to access the deceased donor transplant waiting list, and almost all of these receive a transplant within 4 years of starting dialysis.[6] Iran has also achieved remarkable transplant access through LKD transplantation, in this case with a government initiative regulating and financially supporting living unrelated donation.[9] Although such an approach is not without controversy, its effect has been to develop skills in a generation of surgeons and enable the setting up of a very promising deceased donor scheme.[9]

Although medical factors will always play a role, the importance of psychological, social, and cultural factors in determining differences in rates of transplantation is increasingly being recognized,[10] particularly through the patient's interpretation and assessment of risk associated with transplantation and how it compares with the status quo of dialysis.[1] It has even been suggested that socioeconomic status no longer associates with reduced access once differences in health, functional status, and psychosocial factors such as 'attitudes toward treatment' have been accounted for.[11] If we are to reduce inequity in access to transplantation, we must first understand the educational, psychological, and social milieu of specific patients at specific times. Some of these factors may have more potential for modification than the patient demographics and comorbidity.

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The OSCAR for cardiovascular disease prevention in chronic kidney disease goes to blood pressure control

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Nephropathy progression is slowed and cardiovascular events reduced in patients with stage 3 or higher chronic kidney disease when blood pressure is controlled using combinations of renin–angiotensin system (RAS) blockers with dihydropyridine calcium channel blockers or diuretics. We discuss a trial comparing high-dose RAS blockade with lower-dose RAS blockade combined with a dihydropyridine calcium channel blocker. The primary outcome was cardiovascular events. The combination group had better blood pressure control and fewer total events.

Cardiovascular disease is the leading cause of mortality in patients with chronic kidney disease (CKD), stage 3 or higher; their risk increases as estimated glomerular filtration rate (eGFR) falls. Recently, stage 3 or higher CKD was acknowledged as contributing more risk for all-cause mortality than prior myocardial infarction or diabetes.[1]

Almost all people with CKD, stage 3 or higher, require two or more medications to help achieve guideline recommended blood pressure goals.[2] Before the completion of the Avoiding

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Cardiovascular Events through Combination Therapy in Patients Living with Systolic Hypertension (ACCOMPLISH) trial, no cardiovascular outcome trial ever initiated single-pill combination (SPC) therapy for blood pressure control.[3] The rationale for an SPC antihypertensive treatment was centered on several animal studies demonstrating improved vascular function and nitric oxide release when either the renin–angiotensin system (RAS) blocker benazepril or the dihydropyridine calcium channel blocker amlodipine was given alone, with an additive effect when combined.[4,5] This was not seen when thiazide diuretics were given.[6]

The ACCOMPLISH trial was a randomized, double-blind study involving older hypertensive patients (mean age 68 years) with a history of ischemic heart disease, peripheral vascular disease, stroke, or diabetes that examined the effects on cardiovascular outcomes of treatment with benazepril combined with amlodipine or hydrochlorothiazide.[3] The 2% absolute risk reduction in cardiovascular events seen in the RAS blocker/amlodipine SPC group in the main trial, as well as slowed progression of CKD in those with an eGFR less than 60 ml/min per 1.73 m^2, supports the concept of a blood pressure-independent effect; there was a 1.6-mm Hg difference between groups in systolic blood pressure on 24-h ambulatory blood pressure monitoring, favoring the diuretic.[2,3,7]

The additive effect of a RAS/calcium channel blocker combination on cardiovascular events in CKD was evaluated by Kim-Mitsuyama et al.[8] (this issue) in the OlmeSartan and Calcium Antagonists Randomized (OSCAR) trial. The trial compared the effect of an angiotensin receptor blocker with a calcium channel blocker versus high-dose angiotensin receptor blocker therapy on cardiovascular morbidity and mortality in elderly (mean age 74 years) Japanese people with and without CKD. CKD was defined as an eGFR less than 60 ml/min per 1.73 m^2.

Of 1078 patients in this open-label trial, the authors randomized the 353 patients with CKD (32.7%) to 40 mg olmesartan ($n = 181$) or 20 mg olmesartan with amlodipine or azelnidipine added ($n = 172$). The primary end point was broad and included cardiovascular end points and deterioration of kidney function (doubling of serum creatinine or dialysis), as well as noncardiovascular death. After 3 years of follow-up, the authors concluded, firstly, that blood pressure control was more successful with combination treatment; the mean difference in systolic blood pressure between groups was 3.7 mm Hg, and 17% more patients achieved a blood pressure less than 140/90 mm Hg in the combination group. This finding is already well established in other studies.[9] Secondly, the incidence of cardiovascular deaths and illnesses as well as worsening CKD was lower in the combination group, but this difference was mainly driven by fewer strokes (13 versus 5) and heart failures (8 versus 1). There were no differences in other end points, including CKD progression, as treatment with the angiotensin receptor blocker/calcium channel blocker combination failed to prevent reduction in eGFR compared with high-dose olmesartan. Lastly, the authors concluded that both treatments have similar safety and tolerability profiles and that the higher the blood pressure, the greater the likelihood of events.

This trial provides important information but has many limitations, including that it was open label and was conducted in a homogenous cohort. Consequently, ethnic differences cannot be evaluated; thus, these results may not be generalizable to a broader population. A meta-analysis of open-label randomized trials without blinding demonstrates that lack of double blinding is associated with a 12% overestimation of intervention benefits.[10] Additionally, small sample sizes in studies of interventions with moderate effects have a substantial risk of yielding false-positive or -negative conclusions.

The OSCAR study was not designed to examine the effects of the combination treatment on CKD progression or 24-hour blood pressure control, or the impact of CKD progression on the primary end point. Thus, it is underpowered for any understanding of CKD progression, as the trial is heavily dependent on cardiovascular events. Moreover, it confirms what is already known about elderly patients with stage 3 CKD: that reducing blood pressure to levels below 140/90 mm Hg is associated with significantly reduced risk of heart failure and stroke.[11] Lastly, CKD is appreciated as an independent risk factor for cardiovascular death; thus, this paper does not extend our knowledge about the interaction of diabetes with CKD.[1] Taken together with previous meta-analyses and recent guidelines, OSCAR provides support for the concept that an angiotensin receptor blocker with a calcium antagonist is effective in further reducing cardiovascular events in elderly patients with CKD through better blood pressure control. It does not extend our knowledge, however, as to the slowing of CKD progression or provide insights into new approaches to optimally minimizing the risk of CKD progression in elderly patients with CKD. Moreover, it does not provide information on the use of single-pill combinations to achieve blood pressure goals compared with addition of a second agent.

On the basis of the available data, antihypertensive treatment using SPCs of RAS blockers with dihydropyridine calcium channel blockers yields fewer cardiovascular events and slows CKD progression better in elderly patients than RAS blocker/diuretic SPCs. Moreover, RAS blocker/calcium channel blocker SPCs are better tolerated with better adherence. The OSCAR trial further supports these findings and further supports combination rather than monotherapy in such patients. Future trials need to build on existing knowledge and provide CKD outcomes in elderly patients, as they are the largest growing segment of people starting dialysis in the Western world. In conclusion, the OSCAR goes to achievement of the blood pressure goal of <140/90 mm Hg using combination therapy.

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