Translational Article

Special Issue on the Aging Kidney

Guest Editorial

Introduction to the Aging Kidney

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The changes in kidney function that are coincident with aging is a topic of considerable recent discussion. It is well established that renal function, as measured by one aspect of overall kidney function (GFR), decreases with age in ~30% of the U.S. population (1). These data substantiate the previously held general impression that renal function decreases with age in many persons (2). However, it is important to note that changes in renal function with age vary widely between subjects, and the responses of the individual patient to these changes depend on other environmental, metabolic and systemic stresses placed on the kidney (3). As pointed out in the following group of manuscripts in this issue, it is well known that renal function includes control of many factors, including fluid and electrolytes, calcium/phosphorous metabolism, insulin/glucose metabolism, disposal of ingested and endogenous oxidants, and erythropoiesis (4). In addition, concurrent diseases in other organ systems may directly affect the kidney to function properly independently of age, such as cardiovascular disease, diabetes, liver failure or systemic inflammatory diseases. In turn, the kidneys may directly affect the organ systems such as the cardiovascular system by controlling fluid volume/composition and hormones such as the fibroblast growth factors (5). The effects of the kidney on glucose metabolism are partly mediated by its role in controlling ROS/inflammation, and glucose metabolism plays a major role in changes in multiple organ systems vital to health. Finally, the age of the patient is a major factor. A recent article clearly shows that mortality in octogenarians is directly correlated with renal function (6), whereas this correlation is less evident in younger subjects. While this effect in octogenarians may reflect a bias due to “survivorship,” each age for diseases of any particular associated organ system may be influenced by this same “survivorship” factor.

The purpose of this series of manuscripts chosen for the current issue is to address the question posed by a patient presenting a decrease in some aspect of renal function. In particular, the concern is whether an observed renal function decrease poses a risk of excess morbidity or mortality in the individual patient and whether the decreased renal function or its effects are manageable by currently available interventions.

The first group of manuscripts deals with the epidemiology (7) and significance of decreased renal function in two European countries, Italy (8) and France (9). Bowling and Muntner report that more people are being diagnosed with CKD, and with that, the increased risk of concurrent complications like anemia, acidosis, other metabolic complications, increased mortality, and cardiovascular disease. Additional problems, not previously associated with CKD, like functional decline, cognitive impairment and frailty need to be considered, especially when considering the clinical challenges presented when the patient is more than 80 years old. The Italian study showed that the rate of decline of renal function in ambulatory subjects with CKD was much slower in subjects in the older age category. The number of subjects with diabetes in the 76–87 year old group was quite small, again suggesting that a survivorship bias might be present. The final manuscript in this group is a description of a projected study of France of 581 subject (mean age 82 ± 5 years) with a GFR <14ml/min/1.73m², in which the main topic is when, whether, and on what basis dialysis should be considered. Further, the authors strongly suggest that a Geriatric/Nephrologist collaboration best
serves the patients’ needs. Finally, the contribution by Swidler echoes the need for collaboration between geriatricians and nephrologists in dealing with the aging patient who is approaching endstage renal disease (10). The article provides straightforward guidance.

The next group of articles deals with specific aspects of renal function in aging related to either glomerular or tubular function, the changes due to hypertension, or metabolic events. Dr Wiggins points out the changes that occur in the glomeruli of the aging kidney and discusses the pathophysiology of these changes (11). The article by Sands (4) uses analyses of rat kidneys to show that aging is associated with a decrease in transport proteins that are required for the kidney tubules to be able to concentrate and dilute urine. Since this ability is crucial for the maintenance of the amount and composition of the extracellular fluid volume, their loss in aging could be critical. Similarly, the article by Baylis emphasizes the effects of the loss of the beneficial effects of estrogen after menopause and suggests that this may contribute to the increased risk of cardiovascular and kidney disease in this age group (12). She relates this increased risk to the increase of oxidative stress with aging and shows that this correlates with decreased nitric oxide. The decrease in nitric oxide combined with activation of the renin-angiotensin system appear to coordinately act to decrease renal function in aging. This topic is brought into clinical focus by Oliva and Bakris who give very practical advice on how to manage hypertension in the various decades after the age of 50 (13). They include a brief discussion of the underlying pathophysiology. Importantly, they point out that individualization of treatment plans is particularly important for the patient with hypertension in this age group. An adjacent article by Peron and colleagues studied a group of community-dwelling women over the age of 72 who were receiving treatment for hypertension (14). They found that women receiving peripheral alpha blocker, particularly if they were also receiving loop diuretics, had from four- to eight-fold increase in reported urinary incontinence. These sobering findings suggest that this condition should be asked about in aging women treated for hypertension and that the presence of urinary incontinence may influence the choice of antihypertensive drugs. Since urinary incontinence is a major determinant of health status and independent living, the possibility it might be modifiable in women with treated hypertension is an important observation. The last article in this section deals with another important group of modifiable changes that often accompany aging, namely increased ROS/inflammation. This article by Vlassara and colleagues explores the cause(s) of chronic inflammation in the aged diabetic patient, and how Chr/Infl contributes to decreased renal function (3). The authors provide practical information on how to control chronic inflammatory in aging, CKD and HD patients by simply reducing exposure to advanced glycation endproducts (AGEs) by either a low-AGE diet or an FDA-approved oral drug with a good safety profile in aged subjects. The drug, sevelamer carbonate, binds and removes AGEs introduced into the gut via the food.

In summary, the changes in renal function in aging are not uniform and depend on associated diseases and environmental factors. The articles below provide a number of practical approaches to both the early and late changes in those who have progressively deteriorating kidney function. While the question of which patients require therapy specific to the kidney is undergoing considerable evolution at present, you will find considerable practical advice in these articles.

References