Anatomical Changes in the Aging Kidney

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Introduction

The changes to renal morphology and function in the aging human kidney have been reviewed [1–3]. However, there are many problems in the documentation of the pathological changes in the aging kidney. The confounding variables of hypertension (and ischemia), diabetes, and other co-existing renal diseases are often difficult to dissect out. The renal tissue is frequently not sampled early enough to determine if a primary renal disease is associated with the aging kidney. Most patients with “nephrosclerosis” and/or aging kidneys are not biopsied or autopsied. The nomenclature (definitions), descriptions, and documentation of the morphological changes are often imprecise and usually not quantitated. Focal lesions, especially of the vascular tree, may be missed due to inadequate sampling. There may be “nephron heterogeneity,” which is difficult to quantitate/describe. The terms nephrosclerosis, glomerulosclerosis, arterial sclerosis, arteriolosclerosis, tubular atrophy, and perhaps even interstitial fibrosis are often vaguely used. And finally, there is biologic variability and various rates of structural changes in different ethnicities, countries, and even renal compartments. With these caveats in mind, this chapter tries to summarize the current knowledge of the anatomical changes in the aging human kidney, and, where appropriate, the underlying pathogenetic pathways will be briefly mentioned.

Gross Pathology

Macroscopically, aging kidneys are symmetrically contracted with a fine granular appearance of the subcapsular surface. On average, kidney weight increases from birth to about age 40–50 and then progressively declines, with the most dramatic decrease (about 20–30%) occurring in the seventh and eighth decades [1, 3, 4]. The loss of kidney mass appears to affect the renal cortex more than the medulla, with involution/thinning of the renal cortical parenchyma, which is thought to be related to vascular changes [5, 6].

Approximately one-half of all people 40 years and older have one or more acquired cysts in the kidney [7]. The cysts are generally unilocular and round
to oval, containing clear yellowish fluid. Some believe that simple cysts arise from dilated tubules or glomeruli. Others believe they arise from tubular diverticula found in increasing incidence with aging [8].

The Aging Glomerulus

Many morphological changes have been noted in the human glomerulus with aging [9–21]. These include (1) progressive decline in the number of intact or normal glomeruli, (2) increase in the number/percentage of globally sclerotic glomeruli, especially those of the outer cortical regions initially, (3) abnormal glomeruli with shunts between the afferent and efferent arterioles bypassing the glomeruli, especially the juxtamedullary ones, (4) progressive decrease, and then later increase, in the size of intact glomeruli, (5) focal or diffuse thickening of the glomerular basement membranes, and (6) increased mesangial volume and matrix (i.e., mesangial sclerosis).

The numbers of glomeruli (and hence nephrons) are extremely variable in individuals. Studies by Nyengaard and Bendtsen [15] have suggested that the mean range of the number of glomeruli per kidney is 620,000 ± 250,000, with a range of 333,000 to 1,100,000. Twenty-five percent of the population studied had fewer than 500,000 glomeruli/kidney, whereas 25% of the population had over 740,000 glomeruli/kidney. Likewise, Hughson et al. [16] showed an eightfold difference in the number of glomeruli per person (from 227,327 to 1,825,380 per kidney). On average, females have approximately 15% fewer glomeruli than males [17]. The mean glomerular number is not significantly different between Caucasians and African-Americans, but is significantly lower in Australian aborigines [14,17]. Age is inversely proportional to the number and size of the glomeruli as well as inversely proportional to the kidney weight [14–17]. Thus, humans seem to lose glomeruli with aging.

The relationships of nephron number to birth weight, and to susceptibility to hypertension and renal diseases, have been noted [16–19]. There is a direct linear relationship between the number of glomeruli and birth weight [16]. As birth weight decreases, the number of glomeruli also decreases. In fact, regression coefficient analysis predicts a 257,426-glomeruli increase per kilogram of birth weight. There is an up to eightfold range in glomerular volume among adults, and the glomerular volume is strongly and inversely correlated with the number of glomeruli. In a study of white adults aged 35–59 who died in accidents, Keller et al. [18] have shown that patients with hypertension have approximately 50% fewer glomeruli than matched controls. This study also showed that the volume of glomeruli increases in patients with hypertension compared to matched controls, possibly a result of lower numbers of glomeruli. Based on a stereological study of autopsy kidneys from 140 adults, aged 18–65, who lived in the southeastern United States, Hughson et al. [17] found no relationships between the glomerular number, mean arterial blood pressure (MAP), and birth weights in African-Americans. In contrast, there was a strong correlation of the glomerular number with both birth weight and inversely with MAP in white adults. These data indicate that low nephron number and possibly low birth weight may play a role in the development of hypertension in whites but not in African-Americans.

Samuel et al. [19] analyzed the distributions of volumes of individual glomeruli in the superficial, middle, and juxtamedullary cortex of normal