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CLINICAL RESEARCH

Bowman Capsule Volume and Related Factors in Adults With Normal Renal Function

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Introduction: Alterations in glomerular filtration can considerably influence the dynamics and functions of the Bowman capsule. Despite the potentially important role in maintaining normal renal functions, few studies have focused on Bowman capsule volume in normal human kidneys.

Methods: We analyzed specimens from biopsies performed 1 hour after kidney transplantation from living donors without apparent renal disease. The measurements of all cross-sectional areas of the Bowman capsules and glomerular capillaries were used to estimate the mean Bowman capsule volume (BV) and glomerular capillary volume (GV) in each subject. The G/B ratio was defined as the ratio of GV to BV. The morphometric findings were examined in relation to the clinical findings in donors just before kidney transplantation.

Results: We analyzed 37 adults with a mean creatinine clearance of 111 ml/min. The mean BV and GV of these subjects were $3.74 \pm 1.51 \times 10^6$ μm^3 and $2.35 \pm 0.93 \times 10^6$ μm^3, respectively. Both the BV and GV varied up to 6-fold and were significantly higher in elderly, obese, or hypertensive subjects in comparison to nonelderly, nonobese, or normotensive subjects, whereas the renal function of each subgroup was similar. The G/B ratio (0.63 ± 0.05) was unaffected, and BV and GV were strongly correlated regardless of these clinical factors ($r = 0.980$ [95% confidence interval = 0.961−0.990], $P < 0.001$).

Discussion: In the normal adult kidney, there may be an optimal BV to GV ratio for maintaining effective filtration in a variety of clinical situations, including advanced age, obesity, and hypertension.

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The Bowman capsule is a component of the renal corpuscle, which is an origin of the urinary tubules that constitute the nephrons of the kidney.[1,2] It is composed of the Bowman cavity, a space surrounded by parietal epithelial cell layers and visceral podocytes.[3,4] Physiologically, Bowman capsules are continuously exposed to a large amount of primary urine, which is produced by glomerular capillary filtration. Indeed, approximately 150 L per day of the primary urine are filtered through the glomerular capillaries, and pass through the urinary tubules via the Bowman capsules.[5] It is therefore hypothesized that changes in glomerular filtration can considerably influence the dynamics and functions of the Bowman capsule.

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Glomerular filtration is maintained by ultrafiltration, which is defined by glomerular capillary pressure, plasma osmotic pressure, and Bowman capsule pressure.[6,7] Despite dramatic changes in systemic blood pressure, glomerular capillary pressure is tightly controlled by an automatic regulation system of renal blood flow, including the vasoconstriction of the glomerular afferent and efferent arteries.[8–11] However, it is known that conditions such as obesity, diabetes, or chronic renal failure can impair this regulation system through several mechanisms.[12–14] As a result, these clinical situations may cause glomerular hyperfiltration, a state of overwork in the glomeruli.

The chronic rise in glomerular filtration pressure can be reflected in the enlargement of the glomerular capillaries, such as an increase in the glomerular tuft volume or glomerular diameter. Previous human and animal studies have demonstrated a close link between glomerular hyperfiltration and glomerular hypertrophy.[15] Of note, previous studies have shown the

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significance of glomerular hypertrophy as a predictor of a subsequent loss of renal function in many types of progressive renal disease.[16–19] However, despite the potential importance in the normal renal function, few previous morphometric studies have examined the size of Bowman capsules in normal human kidneys. Thus, the significance in Bowman capsule size differences between individuals remains largely unknown. This study therefore aimed to estimate Bowman capsule volume and to investigate the relationship between Bowman capsule volume and the glomerular capillary volume in subjects with various clinical conditions, including advanced age, obesity, and hypertension, but without apparent renal disease.

METHODS

Patients

In the present study, we investigated biopsy specimens from donor kidneys in living kidney transplantation performed at Jikei Hospital, Tokyo, from 2005 to 2014. The kidney donors were selected according to the Amsterdam Forum guidelines.[20] Subjects with renal manifestations (including apparent renal morphological or functional impairment or urinalysis abnormalities) were excluded at the time of donor selection. To evaluate the renal function, 24-hour urine was collected to investigate the amount of proteinuria, creatinine excretion, and creatinine clearance (CCr). Subjects with a urinary protein excretion of ≥300 mg/d and those with a moderately impaired renal function, defined as a CCr of <80 ml/min, were excluded from the study. Impaired glucose tolerance, defined as hemoglobin A1c (HbA1c) > 6.2% (National Glycohemoglobin Standardization Program [NGSP]) Q5, was a criterion for exclusion. The presence or a history of hypertension was not an exclusion criterion if it was controlled (systolic blood pressure < 130 mm Hg, diastolic blood pressure < 80 mm Hg) by diet or by the use of antihypertensive medications. Renal tissue specimens with < 5 nonsclerotic glomeruli were also excluded based on the results of a previous study.[21]

A total of 59 kidney transplant donors were recruited from the renal biopsy archives during this period. Of these samples, 22 contained <5 nonsclerotic glomeruli and were thus excluded. Finally, 37 biopsies from 37 donors Q6 were included in the present study.

Definitions

"Elderly" was defined as ≥60 years of age.[22] According to the criteria proposed by the Japan Society for the Study of Obesity, a BMI of ≥25 kg/m^2 signified obesity.[23] Hypertension was defined as a systolic blood pressure of >140 mm Hg and/or a diastolic blood pressure of >90 mm Hg, or the use of antihypertensive medications. The estimated glomerular filtration rate (eGFR) was calculated from the serum creatinine (sCr) level using a modified equation for estimating the GFR in Japanese individuals: eGFR = $194 \times \text{age}^{-0.287} \times \text{sCr}^{-1.094}$ ($\times$ 0.739 if female).[24]

Pathological Analysis

The renal biopsies of the kidney transplant donors were performed under direct vision using a needle biopsy gun. All of the biopsy specimens used in this study were obtained after transplantation, at 1 hour after the initiation of blood reperfusion. An 18-gauge biopsy needle was used in all cases. The tissues were embedded in paraffin, cut into 3- to 4-μm sections, and stained with hematoxylin–eosin, periodic acid–Schiff, Masson trichrome, and periodic acid–methenamine silver. The total number of glomeruli identified in the specimens and the percentage of glomeruli affected by global sclerosis were assessed. The area of interstitial fibrosis/tubular atrophy was semiquantitatively evaluated according to the proportion of cortical area involvement.

Morphological Measurements

The areas of all Bowman capsules and glomerular capillaries were measured using a computerized image analyzer (Leica IM500, Leica Microsystems, Germany). Q7 Periodic acid–methenamine silver staining was basically used for the measurements. The Bowman capsule area was defined as the area of the inner side of the glomerular parietal epithelial cell layers. Likewise, the glomerular area was defined as the area of the outer capillary loops of the tuft. Glomeruli that were affected by global glomerulosclerosis were excluded from the analyses. The mean Bowman capsule area (BA) and mean glomerular capillary area (GA) were calculated by averaging all of the measured areas of the Bowman capsules and glomerular capillary loops. The mean Bowman capsule volume (BV) and the mean glomerular capillary volume (GV) were calculated from the measured BA or GA, as follows: $BV = (BA)^{3/2} \times \beta/d \times (f)^{-3}$, $GV = (GA)^{3/2} \times \beta/d \times (f)^{-3}$, where β is a dimensionless shape coefficient ($\beta = 1.38$ for spheres), d is a size distribution coefficient used to adjust for variations in glomerular size ($d = 1.01$), and f is a correction factor used to adjust for the volume shrinkage associated with paraffin fixation ($f = 0.85$).[25–27] The ratio of GV to BV was defined as the G/B ratio and was analyzed in relation to the clinical variables.

Statistical Analysis

Continuous variables were expressed as the mean ± SD. The variables were assessed for normality both visually (normal probability plot) and by inferential

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