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Research Paper

Increased Burden of Vision Impairment and Eye Diseases in Persons with Chronic Kidney Disease — A Population-Based Study

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ABSTRACT

Background: Chronic kidney disease (CKD) has been shown to be associated with diabetic retinopathy (DR) and age-related macular degeneration (AMD), leading causes of blindness in elderly adults in previous studies. However, the association of CKD with visual impairment (VI) is not clear. We aimed to examine the association of CKD with VI and other age-related ocular diseases in a population-based sample of Asian adults.

Methods: We analyzed data from 10,033 adults aged 40–80 years who participated in the Singapore Epidemiology of Eye Diseases (SEED, 2004–11) Study. CKD was defined as an estimated glomerular filtration rate (eGFR) <60 ml/min/1.73 m^2 from serum creatinine. VI was defined as best-corrected visual acuity <20/40 in the better eye. Cataract, retinopathy, DR, glaucoma and AMD were assessed using standardized ocular examination, retinal photography and visual field assessments. The associations of CKD with VI and ocular conditions were examined using logistic regression models adjusted for age, sex, race, smoking, alcohol intake, education status, body mass index, systolic blood pressure, diabetes mellitus, cholesterol levels and cardiovascular disease.

Findings: The prevalence of VI and ocular disease were significantly higher in participants with CKD (36.1% and 84.7%) than in those without (12.9% and 54.3%, both $p < 0.001$). In multivariable models, CKD was significantly associated with VI (odds ratio [95% confidence interval] = 1.34 [1.14–1.58]), any ocular disease (1.28 [1.03–1.61]), cataract (1.24 [1.01–1.52]), any retinopathy (1.77 [1.45–2.15]), and DR (1.94 [1.47–2.54]).

Interpretation: The burden of VI and eye diseases is high among persons with CKD. Our findings suggest that it may be useful to screen for ocular disease and VI in persons with CKD.

1. Introduction

Chronic kidney disease (CKD) is an emerging public health problem associated with adverse cardiovascular and renal outcomes as well as premature deaths (Chronic Kidney Disease Prognosis C et al., 2010). The prevalence of CKD is expected to rise with the aging of the population worldwide. In the US, the prevalence of CKD in adults 30 years or older is projected to increase from 13.2% currently to 14.4% in 2020 and 16.7% in 2030 (Hoerger et al., 2015). In Singapore, the age, sex-standardized prevalence of CKD was reported to be 12.8% (Sabanayagam et al., 2010).

In addition to adverse cardiovascular and renal outcomes, patients with CKD may also be at a higher risk of age-related ocular diseases (Grunwald et al., 2010). Age-related ocular diseases including cataract, retinopathy, glaucoma and age-related macular degeneration (AMD), are leading causes of blindness in middle aged and elderly adults. As the population ages, the prevalence of these diseases is also expected to rise. Age-related ocular diseases share similar cardiovascular risk factors and pathogenic mechanisms including oxidative stress and inflammation, two of the major pathogenic mechanisms underlying CKD. Previous epidemiological studies conducted in the US have shown CKD to be associated with cataract (Klein et al., 1998), diabetic retinopathy (DR) (Wong et al., 2004) and AMD (Klein et al., 2009; Weiner et al., 2011). In a recent study, Grunwald et al. found nearly half of the participants with CKD to have some form of fundus pathology (Grunwald et al., 2010). Hu et al. observed a rise in intraocular pressure and decrease in ocular perfusion pressure in patients on hemodialysis, both being risk factors for glaucoma development and progression (Hu et al., 2013). Intuitively, the burden of visual impairment (VI) should be higher in persons with CKD but the prevalence of VI and other ocular diseases in persons with CKD are unknown, as previous studies did not conduct a complete ophthalmological examination. Besides worsening

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the quality of life (Varma et al., 2006), VI could also contribute to all-cause mortality in persons with CKD, through direct and indirect pathways (Karpa et al., 2009).

In this context, we examined the prevalence and association of CKD with major age-related ocular diseases assessed using a comprehensive eye examination in a population-based sample of Asian adults in Singapore. We hypothesize that persons with CKD would have higher prevalence of ocular diseases and VI than those without CKD.

2. Methods

2.1. Study Population and Design

The data for this study were derived from the Singapore Epidemiology of Eye Diseases (SEED, n = 10,033) Study, comprising of three independent cross-sectional studies encompassing the three major ethnic groups (Chinese, Malays and Indians) in Singapore: the Singapore Malay Eye Study (SiMES, 2004–2006, n = 3280, response rate = 78.7%), the Singapore Indian Eye Study (SINDI, 2007–2009, n = 3400, response rate = 75.6%) and the Singapore Chinese Eye Study (SCES, 2009–2011, n = 3353, response rate = 72.8%). All three studies followed similar protocols and were conducted in the same study clinic (Singapore Eye Research Institute). The detailed methodologies of these studies have been published elsewhere (Foong et al., 2007). In brief, an age-stratified random sampling was used to select ethnic Malays, Chinese and Indians 40 to 80 years of age, who were living in Singapore during each stipulated study period. Each study was conducted in accordance with the Declaration of Helsinki, with written informed consent obtained from all subjects before participation. Ethics approval was obtained from the SingHealth Institutional Review Board. Of the 10,033 study participants, after excluding those with missing information on serum creatinine (n = 434) and other variables (systolic blood pressure, diabetes, cardiovascular disease, total cholesterol, corrected high density lipoprotein, body mass index, smoking status and alcohol intake (n = 165), 9434 were included in the current analysis. In addition, we excluded those with missing values on each of the outcomes separately (AMD: 208 excluded, 9226 included; uncorrected refractive error: 13 excluded, 9421 included; glaucoma: 0 excluded, 9424 included; any retinopathy: 205 excluded, 9229 included; DR: 7251 excluded, 2183 included; cataract: 1581 excluded, 7853 included; VI: 38 excluded, 9396 excluded).

2.2. Study Procedures

Standardized systemic and ocular examinations, interviewer-administered questionnaires, and standard blood investigations were conducted for all participants. Standardized slit-lamp examinations (Haag-Streit model BQ-900; Haag-Streit, Bern, Switzerland) were performed by trained study ophthalmologists after pupil dilatation and the fundus was examined with a 78D lens. A detailed interviewer-administered questionnaire was used to collect relevant demographic data and medical history from all participants. Alcohol drinkers were defined by the consumption of alcohol at least once a week. Cigarette smoking was categorized into current, former and never smoker. Blood pressure was measured with a digital automatic blood pressure monitor (Dinamap model Pro Series DP110X-RW, 100V2; GE Medical Systems Information Technologies, Inc., Milwaukee, WI, USA) after the participants were seated for at least 5 min. The average of the 2 systolic and diastolic blood pressure measurements was used as the systolic and diastolic blood pressure value. Venous blood samples were collected for biochemistry tests, including serum lipids (total cholesterol, high-density lipoprotein cholesterol, and low-density lipoprotein cholesterol), glycosylated hemoglobin A1c (HbA1c), creatinine, and random glucose. Diabetes mellitus was defined as random glucose of 11.1 mmol/L (Alberti and Zimmet, 1998) or more, use of diabetic medication, or a physician diagnosis diabetes mellitus. Cardiovascular disease (CVD) was defined as self-reported myocardial infarction, angina or stroke.

2.3. Assessment of CKD

CKD was defined as an estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m^2, using the US National Kidney Foundation Kidney Disease Outcome Quality Initiative (KDOQI) Working Group definition (National Kidney F, 2002). eGFR was estimated from the serum creatinine concentration (eGFR) (Levey et al., 2009) using the CKD Epidemiology Collaboration (CKD-EPI) equation. Severity of CKD was defined by eGFR categories: ≥60 (stage 1 and 2), 30–59 (stage 3), 29–15 (stage 4) and <15 (stage 5)ml/min/1.73 m^2 (National Kidney F, 2002). Creatinine concentrations were measured by the Jaffe method on the Beckman DXC800 analyzer. The creatinine assay was calibrated to the isotope Dilution Mass Spectroscopy (IDMS) method using the National Institute of Standards and Technology (NIST) Reference material.

2.4. Assessment of VI

Presenting visual acuity was monocularly measured by using a logarithm of the minimum angle of resolution (logmar) number chart (Lighthouse International, New York, USA) at a distance of 4 m. Autorefraction, was performed with an autorefractor machine (Canon RK-5 Auto Ref-Keratometer, Canon Inc. Ltd., Japan). Final refraction was determined by subjective refraction by trained and certified study optometrists. Best-corrected visual acuity after subjective refraction was monocularly assessed and recorded in logMAR scores. VI was defined as best-corrected visual acuity worse than 20/40 in the better eye, based on the US definition (Congdon et al., 2004). Under-corrected refractive error was defined as an improvement of at least 0.2 logMAR (2 lines equivalent) in the best-corrected visual acuity compared with the presenting visual acuity in the better eye.

2.5. Cataract

A digital slit-lamp camera (Topcon model DC-1; Topcon, Japan with FD-21 flash attachment) and a Scheimpflug retroillumination camera (Nidek EAS-1000, Nidek, Japan) were used to photograph the lens through the dilated pupil. Cataract was defined as the presence of nuclear, cortical, or posterior subcapsular cataract using the Wisconsin cataract grading system (Klein et al., 1990).

2.6. DR and any retinopathy

Fundus photography was performed using a digital non-mydriatic retinal camera (Canon CRDGi with a 20Diopter SLR backing, Canon, Japan) using Early Treatment for Diabetic Retinopathy Study (ETDRS) standard field 1 (centered on the optic disk) and ETDRS standard field 2 (centered on the fovea). DR was considered present if characteristic lesions as defined by the Early Treatment Diabetic Retinopathy Study were found on retinal photographs (Wong et al., 2006). DR was evaluated following a standard protocol based on retinal photographs which were graded according to a modified scale from the Airlie House classification system by trained graders (Early Treatment Diabetic Retinopathy Study Research Group, 1991).

2.7. Age-related macular degeneration (AMD)

The presence of AMD signs was graded based on fundus photographs according to the Wisconsin Age-Related Maculopathy Grading System (Kawasaki et al., 2008). The presence of AMD was defined as the presence of either early or late AMD.