Three -Year Incidence and Risk Factors for Retinal Vein Occlusion in Sohag University Hospital

Amin Aboali Hassan

Department Of Ophthalmology, Sohag University Hospital, Faculty of Medicine, Sohag University, Egypt
aminhassan_72@yahoo.com

Abstract: Purpose: To estimate the long-term cumulative incidence and risk factors for retinal vein occlusion (RVO) in a hospital based retrospective study in Sohag University Hospital. **Methods:** In 2007, a total of 1775 individuals aged 40 years or older underwent a baseline eye examination. Of those, 1369 subjects (77.1%) took part in the follow-up eye examination in 2010 and were enrolled in the present study. Each participant underwent a comprehensive examination. The diagnosis of RVO, including branch (BRVO) and central RVO (CRVO), was determined by grading color fundus photographs. Logistic regression analysis was performed to determine risk factors for RVO. **Results:** The 3-year cumulative incidence of RVO was 3.0% (2.7% for BRVO and 0.3% for CRVO). The age-specific cumulative incidence of RVO significantly increased with age (*P* for trend =0.03). After adjusting for age and sex, higher diastolic blood pressure and chronic kidney disease (CKD) were significantly associated with RVO. In multivariate analysis, higher diastolic blood pressure (per 10 mm Hg) (odds ratio [OR], 1.51; 95% confidence interval [CI], 1.14 to 2.01) and CKD (OR, 2.23; 95% CI, 1.02 to 4.89) remained independently significant risk factors for RVO. In stratified analysis, the risk of RVO was higher in subjects with CKD than that in subjects without CKD in both the non hypertension and the hypertension groups. **Conclusions:** These findings suggest that the incidence of RVO is high in Sohag University Hsopital and that higher blood pressure and CKD are independent risk factors for RVO.
[Amin Aboali Hassan. **Three -Year Incidence and Risk Factors for Retinal Vein Occlusion in Sohag University Hospital.** *Life Sci J* 2013; 10(3): 1840-1845] (ISSN: 1097-8135). http://www.lifesciencesite.com. 274

Keywords: Incidence; Risk Factor; Retinal Vein Occlusion; Hospital

1. Introduction

Retinal vein occlusion (RVO) is one of the causes for significant loss of vision in elderly populations in developing countries.[1] Despite the magnitude of this problem, the available treatment options remain limited.[2,3] Furthermore, RVO has also been associated with increased risk of cardiovascular disease.[4–6] It is thus very important to determine the prevalence of RVO and to identify its systemic risk factors to develop preventive measures for the disease. To date, several population- based studies,[6–11], have provided valuable information on the incidence and risk factors for RVO. The risk factors reported include hypertension, [6–11] diabetes,[10] smoking habits,10 dyslipidemia,[7,9] and a history of angina.[9] However, there have been only a limited information on the long-term risk of RVO is nonexistent in middle east including Egypt. The purpose of this article was to examine the 3-year incidence of RVO and its risk factors in a retrospective study of patients attending Outpatient clinic of ophthalmology.

2, Material and Methods

Study Population

In 2007, a total of 1775 individuals (688 males, 1087 females) aged 40 years or older underwent a baseline eye examination. Of those, 1404 subjects (79.1%) took part in the follow- up eye examination in 2010. After excluding 35 subjects with RVO at the baseline examination, the remaining 1369 subjects (508 males, 861 females, 77.1% of the original) were enrolled in the present study.

Assessment of RVO

The methods used for the baseline eye examination included comprehensive ophthalmic examination, including stereoscopic fundus examination using indirect ophthalmoscopy, and examination with a slit-lamp biomicroscope with a "Volk 78 D lens" (Volk Optical Inc., Mentor, OH) after pupil dilatation with 1.0% tropicamide and 5% phenylephrine. Fundus photographs (45°) were taken using a fundus camera (Topcon TRC NW-6SF; Topcon). In the 3-year follow-up eye examination, fundus photographs (45°) were taken using digital fundus camera (Topcon TRC NW-6SF; Topcon). In both examinations, we took one photographic field centered on a point midway between the temporal edge of the optic disc and the fovea in both eyes and used a similar masked photographic grading technique. The presence of RVO was determined based on the grading of fundus examinations by indirect ophthalmoscopy, slit-lamp, and color fundus photographs. All photographs were evaluated by retinal specialists (MY and TI) who were masked to participant data. The presence or absence of either central or branch RVO (CRVO or BRVO, respectively) was defined according to a standardized

protocol.[10,16] Recent CRVO was characterized by widespread scattered superficial or deep retinal hemorrhages with or without optic disc hyperemia or edema, venous dilatation, retinal edema, or occluded or sheathed veins. Old CRVO was diagnosed by the presence of anastomotic vessels on the disc. For hemispheric RVO, these signs were present in the upper or lower retinal half, corresponding to the branch of the central vein in which the occlusion occurred. BRVO was characterized by retinal hemorrhages occurring within the retinal sector corresponding to the blood supply sector of the occluded venule and by scattered superficial and deep retinal hemorrhages, venous dilatation, intraretinal microvascular abnormalities, and occluded and sheathed retinal venules. Old BRVO was characterized by the presence of collateral vessels or intraretinal microvascular abnormalities in a retinal sector. The presence of any RVO was defined as the presence of BRVO or CRVO in either eye.

Assessment of Other Variables

Blood pressure was measured three times from subjects in a sitting position after each subject had rested for at least 5 minutes, and the average of the three measurements was used for the analysis. Hypertension was defined as a systolic blood pressure > 140 mm Hg, diastolic blood pressure > 90 mm Hg, or current use of antihypertensive medication. Body height and weight were measured from subjects in light clothing without shoes, and the body mass index (kg/m^2) was calculated.

Serum total cholesterol levels were measured. Plasma glucose concentrations were determined. Diabetes was defined by a 75-g oral glucose tolerance test, by fasting (>110 mg/dl) or postprandial (> 200 mg/dl) blood glucose levels or by the use of hypoglycemic agents. Hematocrit levels were determined.

At the baseline examination, fresh voided urine samples were tested by the dipstick method, and proteinuria was defined as ≥ 1+ We defined CKD as the presence of proteinuria Information on smoking habits and alcohol intake was obtained using a standard questionnaire administered by trained interviewers at the initial examination. Subjects were classified either as current habitual users or as nonusers.

Statistical Analysis

We calculated the 3-year incidences of RVO. Incident RVO was defined by the appearance at follow-up of either BRVO or CRVO in either eye of persons in whom no BRVO or CRVO was present at baseline. We examined the relationships between risk factors at baseline and the incidence of RVO. We considered the following 11 possible risk factors for RVO: age, sex, hypertension, systolic blood pressure, diastolic blood pressure, diabetes, total cholesterol, body mass index, chronic kidney disease (CKD), smoking habits, and hematocrit.

Age, systolic blood pressure, diastolic blood pressure, total cholesterol, body mass index, and hematocrit were treated as continuous variables and the others as categorical variables. Each categorical variable was coded as either 1 or 0, depending on the presence or absence of the factor, respectively. Mean values were compared by the Student's *t*-test and frequencies by x^2 test. We estimated the age adjusted and multivariate odds ratios (ORs) and their 95% confidence intervals (CIs) of each potential risk factor by using a logistic regression analysis. Heterogeneity in the relationship between subgroups of hypertension status was tested by adding a multiplicative interaction term to the relevant logistic model. A statistical software package (SPSS version 12.0; SPSS, Inc, Chicago, IL) was used to perform all statistical analyses. A two-sided value of $P < 0.05$ was considered statistically significant.

3. Results

Table 1 shows the comparison of baseline characteristics between subjects with and without RVO. Subjects with RVO were older than those without RVO, but the proportion of males was not different. The mean values of systolic and diastolic blood pressures and the frequencies of hypertension and CKD were higher in subjects with RVO than values in subjects without RVO.

The age-specific 3-year cumulative incidence of RVO is shown in Table 2. Of the 1369 subjects at risk, 41 (3.0%) developed RVO during the follow-up. The cumulative incidence of BRVO was 2.7%, and that of CRVO was 0.3%. The age-specific cumulative incidence of RVO significantly increased with advancing age in all subjects (P for trend =0.03). This trend was observed for females ($P = 0.01$), but not for males ($P = 0.75$).

Table 3 presents the results of age- and sex-adjusted and multivariate-adjusted logistic regression analyses of risk factors for the development of RVO. After adjusting for age and sex, higher diastolic blood pressure (per 10 mm Hg) (OR, 1.55; 95% CI, 1.16 to 2.05) and CKD (OR, 2.39; 95% CI, 1.10 to 5.20) were significant risk factors for the development of RVO. In multivariate analysis, diastolic blood pressure (OR, 1.51; 95% CI, 1.14 to 2.01) and CKD (OR, 2.23; 95% CI, 1.02 to 4.89) remained independently significant risk factors for RVO.

Table 4 shows the age- and sex-adjusted ORs of elevated diastolic blood pressure and CKD for the development of RVO by hypertension status.

Table 1. Characteristics of Study Population with or without development of RVO: Sohag Study, 2007

Variable	Non-RVO (*n*= 1328)	RVO (*n*= 41)
Age, y	60.0 ± 10.0	63.0 ± 8.0*
Sex, male %	37.0	39.0
Hypertension, %	40.7	56.1*
Systolic blood pressure, mm Hg	132.0 ±21.0	140.0 ± 24.0*
Diastolic blood pressure, mm Hg	78.0 ±10.0	82.0 ± 12.0**
Diabetes, %	10.7	14.6
Total cholesterol, mM	5.4 ± 0.9	5.3 ± 0.7
Body mass index, kg/m2	23.2 ±3.2	23.6 ±3.2
Chronic kidney disease, %	10.2	24.4**
Hematocrit, %	40.2 ±3.9	40.6 ±3.8
Smoking habits, %	16.1	22.0

Values are expressed as means ± SD or percentages. *$P < 0.05$, **$P <0.01$, vs. non-RVO.

In the hypertensive group, higher diastolic blood pressure and CKD significantly increased the risk of RVO, whereas no such associations were observed in the non hypertensive group, probably due to the small number of RVO cases. The heterogeneity of the two groups was not significant for elevated diastolic blood pressure (*P* for heterogeneity _ 0.69) and CKD (0.99).

Table 2: Age-Specific 3-Year Cumulative Incidence of RVO by Sex: Sohag Study, 2007-2010

		Number of Cases (%)			
Group/Age (y)	**Population at Risk**	**Branch RVO**	**Central RVO**	**All RVO**	***P* for Trend**
Males					
40-49	73	2 (2.7)	0 (0.0)	2 (2.7)	
50-59	136	4 (2.9)	0 (0.0)	4 (2.9)	
60-69	183	4 (2.2)	2 (1.1)	6 (3.3)	
70+	116	4 (3.5)	0 (0.0)	4 (3.5)	0.75
Females					
40-49	177	1 (0.6)	0(0.0)	1 (0.6)	
50-59	253	6 (2.4)	0 (0.0)	6 (2.4)	
60-69	172	10 (3.7)	1 (0.4)	11 (4.0)	
70+	159	6 (3.8)	1 (0.4)	7 (4.4)	0.01
All					
40-49	250	3 (1.2)	0 (0.0)	3 (1.2)	
50-59	389	10 (2.6)	0 (0.0)	10 (2.6)	
60-69	455	14 (3.1)	3 (0.7)	17 (3.7)	
70+	275	10 (3.6)	1 (0.4)	11 (4.0)	0.03
Total	1369	37 (2.70)	4 (0.29)	41 (2.99)	

Table 3: Age- and Sex-Adjusted and Multivariate-Adjusted Odds Ratio of Risk Factors for RVO: Sohag Study, 2007-2010

	Odds Ratio (95% Confidence Interval)			
Variable	**Age- and Sex-Adjusted**	***P***	**Multivariate Model**	***P***
Age, per 1 year			1.03 (0.99–1.06)	0.14
Sex, Males			1.19 (0.62–2.30)	0.60
Hypertension	1.61 (0.83–3.11)	0.16		
Systolic blood pressure, per 10 mm Hg	1.15 (0.99–1.32)	0.06		
Diastolic blood pressure, per 10 mm Hg	1.55 (1.16–2.05)	0.003	1.51 (1.14–2.01)	0.004
Diabetes	1.28 (0.52–3.12)	0.59		
Total cholesterol, per 1 mM	0.90 (0.61–1.31)	0.58		
Body mass index, per 1 kg/m2	1.04 (0.94–1.14)	0.45		
Chronic kidney disease	2.39 (1.10–5.20)	0.03	2.23 (1.02–4.89)	0.04
Hematocrit, per 10%	1.44 (0.52–4.00)	0.48		
Smoking habits	1.71 (0.73–4.01)	0.22		

Table 4: Association of Diastolic Pressure and Chronic Kidney Disease (CKD) with the Development of RVO by Hypertension Status: Sohag Study, 2007-2010

Crude Incidence of RVO					
Group	**Population at Risk (*n*)**	**Cases *n* (%)**	**Age- and Sex-Adjusted Odds Ratio (95% Confidence Interval)**	***P***	***P* for Heterogeneity**
Hypertension(-) Diastolic blood pressure, per 10 mm Hg	805	18 (2.2)	1.41 (0.72-2.77)	0.31	
Hypertension(+) Diastolic blood pressure, per 10 mm Hg	564	23 (4.1)	1.58 (1.03-2.42)	0.034	0.69
Hypertension(-)					
Non-CKD	745	15 (2.0)	1	0.38	
CKD	60	3 (5.0)	1.79 (0.48-6.74)		
Hypertension(+)			1		0.99
Non-CKD	478	16 (3.3)	2.86 (1.07-7.63)	0.035	
CKD	86	7 (8.1)			

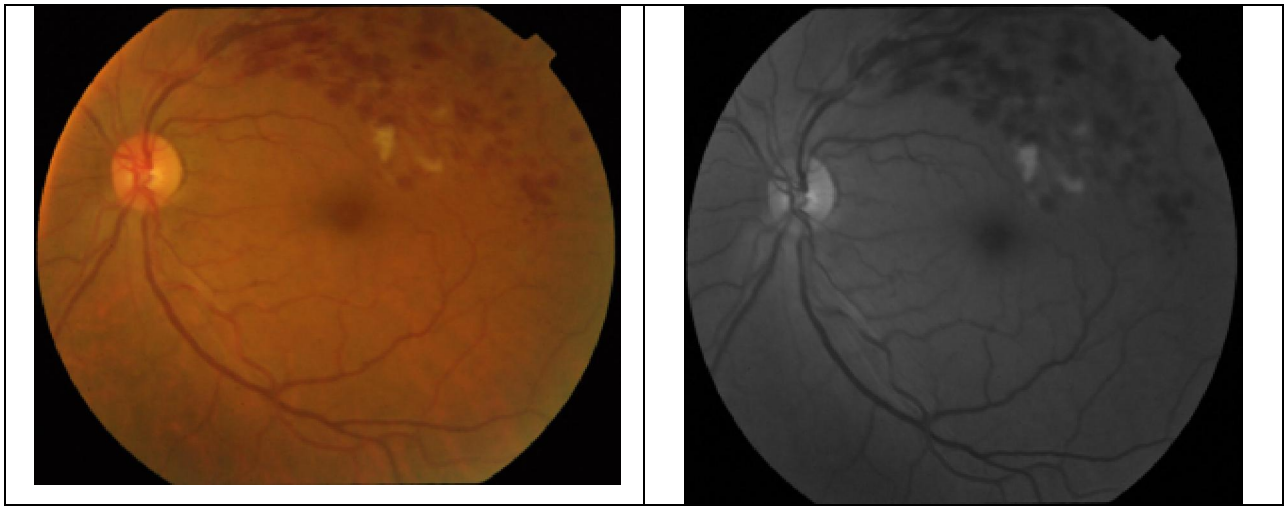

Figure 1: A case of BRVO, fundus picture on left and red free picture on right.

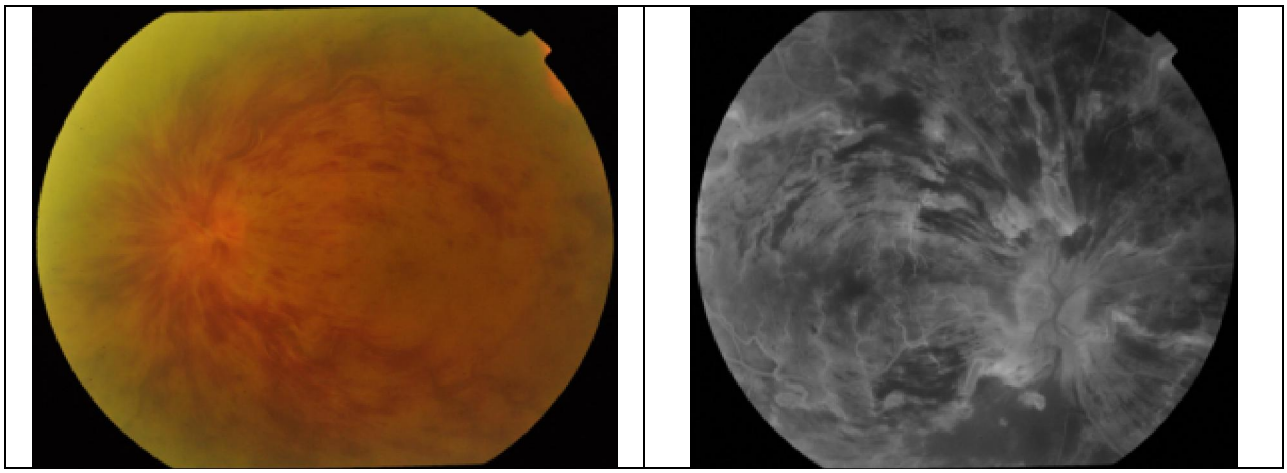

Figure 2: A case of CRVO, fundus picture on left and red free picture on right.

4. Discussion

The present study showed a 3-year cumulative incidence of RVO was 3.0% and found that higher diastolic blood pressure and CKD were independent risk factors for the development of RVO in Sohag population. To our knowledge, this is the first hospital-based study that investigated the incidence and risk factors for RVO in Sohag.

A few cohort studies have reported the cumulative incidence of RVO. In the Beaver Dam Eye Study (University of Wisconsin-Madison), the 15-year cumulative incidences of

BRVO and CRVO were 1.8% and 0.5%, respectively.[16] Similar findings were obtained from the 10-year follow-up of the Blue

Mountains Eye Study in Australia (BRVO, 1.2% and CRVO,0.4%).[8] In Japan, one cohort study reported a 10-year RVO incidence of 0.4%.[20]

Therefore, it has been believed that the incidence of RVO was much lower in Japanese than that in Caucasians. In that Japanese study, however, the study population was very small (n = 245), and the follow-up rate was very low (19.6%).

In our hospital-based study, the 3-year incidence of RVO was 3.0% (BRVO, 2.7% and CRVO, 0.3%). This finding suggests that the incidence of RVO in Sohag is twofold higher than that in Caucasians.

The present study found that higher diastolic blood pressure was significantly associated with RVO and that higher systolic blood pressure was marginally associated with RVO.

The risk of elevated diastolic blood pressure for RVO was higher in both the hypertensive and the non hypertensive groups (P for heterogeneity = 0.69), indicating the close association of diastolic blood pressure and RVO. Although the etiology and pathogenesis of RVO are largely unknown, the consistent association with elevated blood pressure found in this study is in accordance with the findings from many other studies,[6–8,10–12] confirming the blood pressure–related nature of the disease. In contrast, the baseline hypertension was not significantly associated with RVO. This may, in part, occur because of receiving antihypertensive medication in hypertensive persons. This suggests that uncontrolled hypertension may be a more important contributing factor to RVO. Therefore, subjects with elevated blood pressure should be considered a high-risk population of RVO. Strict control of elevated blood pressure may be important in preventing the disease.We found that a CKD was associated with RVO, independent of age, sex, and diastolic blood pressure. Previously only two population-based cohort studies have reported on the association between renal dysfunction and RVO, and the results have been inconsistent. In the Blue Mountains Eye Study, the serum creatinine level was not associated with the development of RVO in a 10-year follow-up period.[8] On the other hand, higher serum creatinine levels constituted a significant risk factor for RVO over 15 years of follow-up in the Beaver Dam Eye Study; persons with elevated creatinine levels (≥1.4 mg/dL) were shown to have a 60% higher risk of RVO.16 In our study, CKD increased the risk of developing RVO by 2.2-fold even after adjustment for other confounding factors. These discrepancies in the association between renal dysfunction and RVO may be partly due to differences in ethnicity, study populations, or study methods. Our findings provide important evidence of a link between CKD and RVO and suggest that CKD affects ocular circulation.

Renal dysfunction and RVO are both closely related to hypertension.[6,21] This fact indicates concomitant damage in the retinal and renal vasculature by hypertension. In this study, however, CKD was an independent risk factor for the development of RVO, even after adjustment for age, sex, and diastolic blood pressure. We also demonstrated that the risk of RVO is higher in subjects with CKD than that in subjects without CKD in both the non hypertension and the hypertension groups (P for heterogeneity = 0.99). These findings suggest that CKD was an independent risk factor for the development of RVO regardless of hypertension status, and that hypertension is not a key factor connecting CKD and RVO. It is well recognized that renal arteriosclerosis and glomerular sclerosis are closely related to systemic atherosclerosis.[22] A previous population-based autopsy study of Hisayama residents also indicated that CKD was significantly associated with the severity of coronary atherosclerosis.[23] Based on these findings, it is speculated that CKD is a strong risk factor for systemic arteriosclerosis, including retinal arteriosclerosis, and that retinal sclerotic arteriolar walls may compress the underlying veins at arteriovenous crossings, leading to reduced blood flow, which in turn could facilitate the development of a thrombus and downstream venous occlusion and thereby of RVO.

The several strengths of our study include its longitudinal hsopital-based design, long follow-up, and masked grading of retinal photographs from both eyes after pupil dilatation.

However, several limitations merit consideration. First, we ascertained RVO cases by using one photographic field per eye, whereas in most previous population-based studies, at least two photographic fields were taken per eye. This could have resulted in underestimation of the prevalence of RVO in our study, if peripheral lesions were overlooked. However, we diagnosed RVO with

fundus examinations by indirect ophthalmoscopy, slit-lamp, and color fundus photographs in both eyes after pupil dilatations. Therefore, RVO could bediagnosed with accuracy.

Conclusions:

These findings suggest that the incidence of RVO is high in Sohag university hospital in upper Egypt and that higher blood pressure and CKD are independent risk factors for RVO.

References

1. Klein R, Wang Q, Klein BE, Moss SE, Meuer SM. The relationship of age-related maculopathy, cataract, and glaucoma to visual acuity. *Invest Ophthalmol Vis Sci.* 1995;36:182–191.
2. McIntosh RL, Mohamed Q, Saw SM, Wong TY. Interventions for branch retinal vein occlusion: an evidence-based systematic review. *Ophthalmology.* 2007;114:835–854.
3. Mohamed Q, Mclntosh RL, Saw SM, Wong TY. Interventions for central retinal vein occlusion: an evidence-based systematic review. *Ophthalmology.* 2007;114:507–519.
4. Cugati S, Wang JJ, Knudtson MD, *et al.* Retinal vein occlusion and vascular mortality: pooled data analysis of 2 population-based cohorts. *Ophthalmology.* 2007;114:520–524.
5. Baker ML, Hand PJ, Wang JJ, Wong TY. Retinal signs and stroke: revisiting the link between the eye and brain. *Stroke.* 2008;39: 1371–1379.
6. Wong TY, Larsen EKM, Klein R, *et al.* Cardiovascular risk factors for retinal vein occlusion and arteriolar emboli: the Atherosclerosis Risk in Communities and Cardiovascular Health studies. *Ophthalmology.*2005;112:540–547.
7. Cheung N, Klein R, Wang JJ, *et al.* Traditional and novel cardiovascular risk factors for retinal vein occlusion: the multiethnic study of atherosclerosis. *Invest Ophthalmol Vis Sci.* 2008;49:4297–4302.
8. Cugati S, Wang JJ, Rochtchina E, Mitchell P. Ten-year incidence of retinal vein occlusion in an older population: the Blue Mountains Eye Study. *Arch Ophthalmol.* 2006;124:726–732.
9. Lim LL, Cheung N, Wang JJ, *et al.* Prevalence and risk factors of retinal vein occlusion in an Asian population. *Br J Ophthalmol.* 2008;92:1316–1319.
10. Klein R, Klein BEK, Moss SE, Meuer SM. The epidemiology of retinal vein occlusion: the Beaver Dam Eye Study. *Tr Am Ophth Soc.* 2000;98:133–143.
11. Kawasaki R, Wong TY, Wang JJ, Kayama T, Yamashita H. Body mass index and vein occlusion. *Ophthalmology.* 2008;115:917–918.
12. Liu W, Xu L, Jonas JB. Vein occlusion in Chinese subjects. *Ophthalmology.* 2007;114:1795–1796.
13. Katsuki S. Epidemiological and clinicopathological study on cerebrovascular disease in Japan. *Prog Brain Res.* 1966;21:64–89.
14. Kubo M, Kiyohara Y, Kato I, *et al.* Trends in the incidence, mortality, and survival rate of cardiovascular disease in a Japanese community: the Hisayama Study. *Stroke.* 2003;34:2349–2354.
15. Yasuda M, Kiyohara Y, Arakawa S, *et al.* Prevalence and systemic risk factor of retinal vein occlusion in a general Japanese population: the Hisayama Study. *Invest Ophthalmol Vis Sci.* 2010; 51:3205–3209.
16. Klein R, Moss SE, Meuer SM, Klein BEK. The 15-year cumulative incidence of retinal vein occlusion: the Beaver Dam Eye Study. *Arch Ophthalmol.* 2008;126:513–518.
17. Imai E, Horio M, Nitta K, *et al.* Estimation of glomerular filtration rate by the MDRD study equation modified for Japanese patients with chronic kidney disease. *Clin Exp Nephrol.* 2007;11:41–50.
18. Matsuo S, Imai E, Horio M, *et al.* Revised equations for estimated GFR from serum creatinine in Japan. *Am J Kidney Dis.* 2009;53: 982–992.
19. Levey AS, Coresh J, Balk E, *et al.* National Kidney Foundation practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *Ann Intern Med.* 2003;139:137–147.
20. Kashiwagi K, Shibuya T, Tukahara S. De novo age-related retinal disease and intraocular-pressure changes during a 10-year period in a Japanese adult population. *Jpn J Ophthalmol.* 2005;49:36–40.
21. Elsayed EF, Tighiouart H, Griffith J, *et al.* Cardiovascular disease and subsequent kidney disease. *Arch Intern Med.* 2007;167:1130– 1136.
22. Keane WF, Kasiske BL, O'Donnell MP. Lipid and progressive glomerulosclerosis: a model analogous to atherosclerosis. *Am J Nephrol.* 1988;8:261–271.
23. Nakano T, Ninomiya T, Sumiyoshi S, *et al.* Association of kidney function with coronary atherosclerosis and calcification in autopsy samples from Japanese elders: the Hisayama Study. *Am J KidneyDis.* 2010;55:21–23.

8/12/2013