Conclusions

Subjects who have both high blood pressure and higher hematocrit should be considered a high-risk population of RVO.

Department of Ophthalmology, Kyushu University

Prevalence and systemic risk factors of retinal vein occlusion in a general Japanese population: the Hisayama Study

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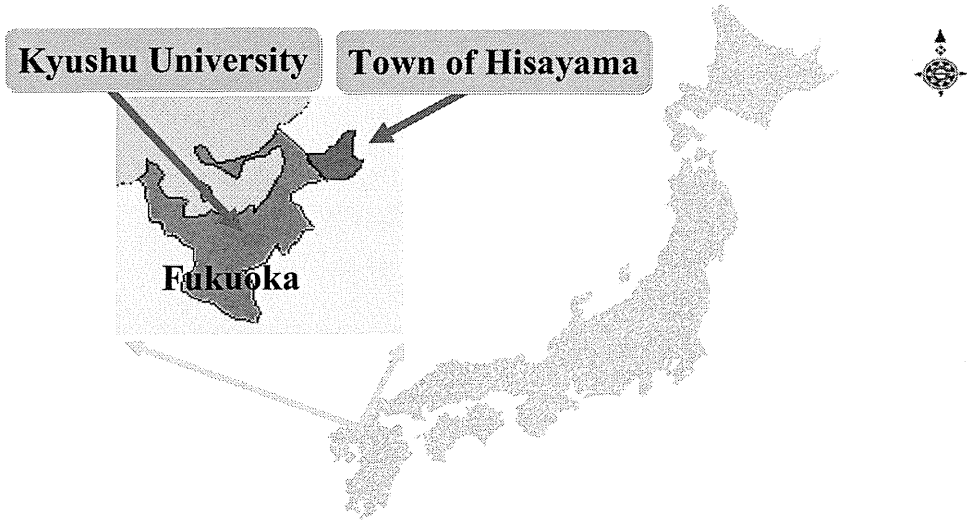
Financial Disclosure

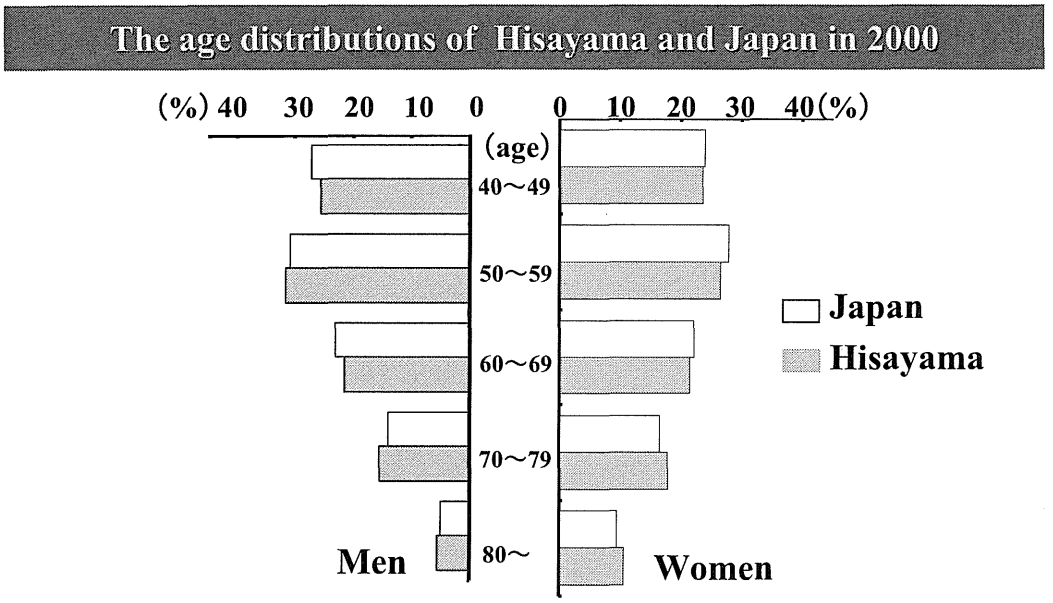
We do not have any financial interests or relationships to disclosure.

The Hisayama Study

The Hisayama Study is an ongoing long-term cohort study on cardiovascular disease and its risk factors in the town of Hisayama adjoining Fukuoka City, a metropolitan area in southern Japan. As a part of the study, an epidemiological study of eye disease among residents of the town has been underway since 1988.

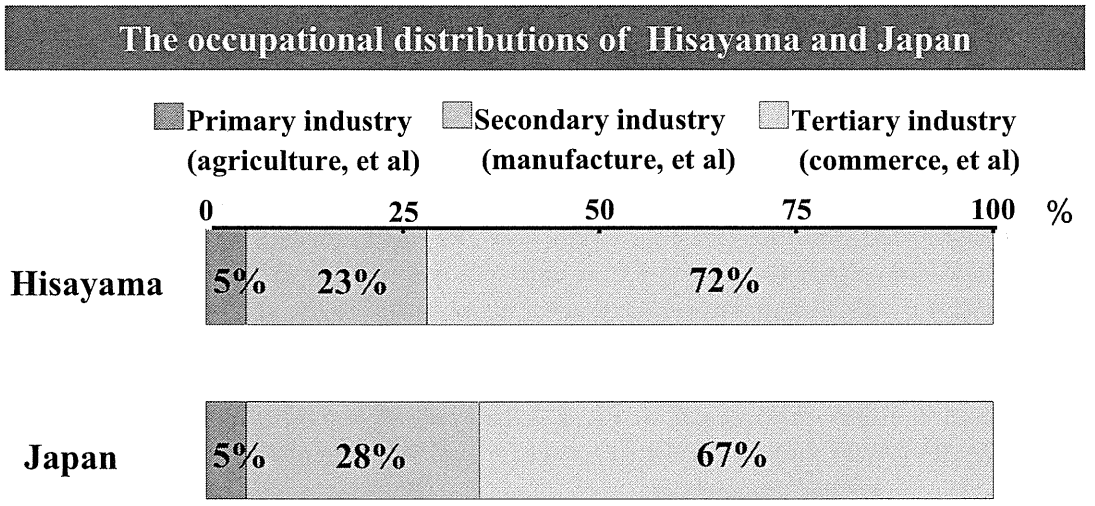


The Hisayama Study



The age distributions of the Hisayama population are similar to those of Japan.

The Hisayama Study



The occupational distributions of the Hisayama population are similar to those of Japan.

Purpose

The aim of this study was to examine the prevalence of retinal vein occlusion (RVO) and its systemic risk factors in a general Japanese population.

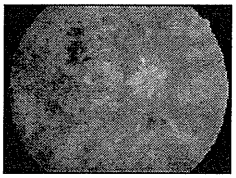
Study Population

In 1998, a total of 1,775 residents of the town (688 men and 1,087 women) aged 40 years or older underwent an ophthalmic examination for the present study.

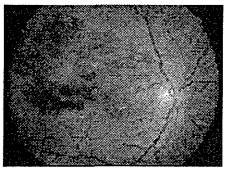
Methods : Definition of RVO

We took one photograph in both eyes. The presence of RVO was determined based on color fundus photographs. The presence or absence of either central or branch RVO was defined according to a standardized protocol.

Briefly, recent central RVO was characterized by retinal edema, optic disc hyperemia or edema, scattered superficial and deep retinal hemorrhages, and venous dilation. Old central RVOs were characterized by occluded and sheathed retinal veins or vascular anastomosis at the optic disc. Branch RVOs involved a more localized area of the retina in the sector of the obstructed venule and were characterized by scattered superficial and deep retinal hemorrhages, venous dilation, intraretinal microvascular abnormalities, and occluded and sheathed retinal venules. The presence of any RVO was defined as the presence of branch or central RVO in either eye.



central RVO



branch RVO

Methods : Statistical methods

1. We considered the following eighteen possible risk factors for RVO: age, sex, systolic and diastolic blood pressure, hypertension, total cholesterol, HDL cholesterol, triglycerides, body mass index, diabetes mellitus, WBC count, platelet count, hematocrit, ECG abnormalities, history of cardiovascular disease, smoking habits, alcohol intake, and regular exercise.

2. We estimated the age- and sex-adjusted and multivariate-adjusted odds ratios (ORs) and their 95% confidence intervals (CIs) for each potential risk factor by using a logistic regression analysis.
   The SAS software package (SAS Institute, Cary, NC) was used to perform all statistical analyses. A two-sided p-value of < 0.05 was considered statistically significant.

Results 1

Characteristics of the study population by sex, the Hisayama Study, 1998

Variables	Men (n=688)	Women (n=1,087)
Age (year)	63±10	61±11
Systolic blood pressure (mmHg)	135±21	132±22
Diastolic blood pressure (mmHg)	80±11	76±10
Hypertension (%)	50.2	41
Total cholesterol (mmol/l)	5.02±0.87	5.51±0.85
High-density lipoprotein cholesterol (mmol/l)	1.39±0.33	1.58±0.36
Triglycerides (mmol/l)	1.32 (0.63-3.65)	1.14 (0.58-2.57)
Body mass index (kg/m^2)	23.2±3.0	23.0±3.4
Diabetes (%)	17.9	9.2
White blood cells ($\times 10^3$/mm^3)	6.3±1.7	5.5±1.3
Platelets ($\times 10^4$/mm^3)	21.1±5.1	22.3±5.2
Hematocrit (%)	43.1±3.6	38.3±3.1
ECG abnormalities (%)	20.2	15.5
History of cardiovascular disease (%)	6.5	2.9
Smoking habits (%)	37.5	4.8
Alcohol intake (%)	65.6	18.4
Regular exercise (%)	17.8	16.3

•Values are expressed as the means ± standard deviation or percentages.
•Geometric mean value and 95% prediction interval of triglycerides are shown because of the skewed distribution.

Results 2

Age-specific prevalence of retinal vein occlusion by sex, the Hisayama Study, 1998

Age range (years)	Men			Women			All subjects			
	population at risk, N	branch RVO N (%)	central RVO N (%)	population at risk, N	branch RVO N (%)	central RVO N (%)	population at risk, N	branch RVO N (%)	central RVO N (%)	All RVO N (%)
40-49	92	0(0.0)	0(0.0)	201	0(0.0)	0(0.0)	293	0(0.0)	0(0.0)	0(0.0)
50-59	154	2(1.3)	0(0.0)	284	5(1.8)	0(0.0)	438	7(1.6)	0(0.0)	7(1.6)
60-69	231	5(2.2)	3(1.3)	335	10(3.0)	0(0.0)	566	15(2.7)	3(0.5)	18(3.2)
70-79	178	7(3.9)	0(0.0)	212	2(0.9)	0(0.0)	390	9(2.3)	0(0.0)	9(2.3)
80+	33	2(6.1)	0(0.0)	55	2(3.6)	0(0.0)	88	4(4.6)	0(0.0)	4(4.6)
Total	688	16(2.3)	3(0.4)	1087	19(1.8)	0(0.0)	1775	35(2.0)	3(0.2)	38(2.1)
p for trend		*p*=0.01	*p* =0.87		*p*=0.15			*p*=0.005	*p*=0.66	*p*=0.005

•RVO, retinal vein occlusion

Results 3

Age- and sex-adjusted and multivariate-adjusted odds ratios of risk factors for retinal vein occlusion, the Hisayama Study, 1998

Risk factor	Age- and sex-adjusted OR	95%CI	Multivariate-adjusted OR	95%CI
Age (per 10 years)			1.47*	1.04-2.08
Sex (male)			0.93	0.42-2.07
Systolic blood pressure (per 10 mmHg)	1.23**	1.07-1.41		
Diastolic blood pressure (per 10 mmHg)	1.46*	1.09-1.97		
Hypertension	4.53**	1.94-10.6	4.25**	1.82-9.94
Total cholesterol (per 1 mmol/l)	1.20	0.83-1.74		
High-density lipoprotein cholesterol (per 1 mmol/l)	2.22	0.94-5.25		
Triglycerides (per 1 mmol/l)	0.63	0.36-1.10		
Body mass index (per 1 kg/m^2)	1.04	0.94-1.15		
Diabetes	0.65	0.23-1.87		
White blood cells (per $10^3/mm^3$)	1.15	0.94-1.40		
Platelets (per $10^4/mm^3$)	0.94	0.88-1.01		
Hematocrit (per 10 %)	3.09*	1.13-8.46	1.10*	1.00-1.22
ECG abnormalities	1.57	0.76-3.26		
History of cardiovascular disease	0.91	0.21-3.91		
Smoking habits	0.95	0.39-2.34		
Alcohol intake	1.42	0.67-3.01		
Regular exercise	1.24	0.58-2.68		

•OR, odds ratio; CI, confidence interval; *p<0.05, **p<0.01

Results 4

Age- and sex-adjusted odds ratios of retinal vein occlusion according to blood pressure levels and quartiles of hematpcrit, the Hisayama Study, 1998

Risk factor level	Population at risk, N	Cases N	Age- and sex-adjusted OR (95% CI)	*p* value for trend
Blood pressure level				
Optimal	469	1	1.00 (reference)	<0.001
Normal	276	1		
High-normal	240	5	6.81 (1.30-35.6)*	
Hypertension	790	31	11.9 (2.78-50.9)**	
Hematocrit				
First quartile < 37.7	436	5	1.00 (reference)	0.004
Second quartile 37.7-39.9	447	7	1.40 (0.44-4.46)	
Third quartile 40.0-42.6	445	8	1.81 (0.58-5.70)	
Fourth quartile ≥ 42.7	446	18	6.03 (1.85-19.7)*	

According to the 2007 European Society of Hypertension (ESH) and European Society of Cardiology (ESC) Practice Guidelines, blood pressure levels were categorized as follows:

Optimal blood pressure (systolic blood pressure <120mmHg and diastolic blood pressure <80mmHg)
Normal blood pressure (120 to 129/80 to 84 mmHg)
High-normal blood pressure (130 to 139/85 to 89 mmHg),
Hypertension (≥140/≥90 mmHg or current use of antihypertensive medication).

•OR, odds ratio; CI, confidence interval; *p<0.05, **p<0.01

Results 5

Age- and sex-adjusted odds ratios of retinal vein occlusion according to the presence and absence of hypertension and hematpcrit levels, the Hisayama Study, 1998

	Population at risk, N	Cases N	Age- and sex-adjusted OR (95% CI)	*p*
Normal blood pressure + Low hematocrit	595	1	1.00 (reference)	
Normal blood pressure + High hematocrit	150	1	4.81 (0.28-82.2)	0.28
High blood pressure + Low hematocrit	742	20	11.9 (1.57-90.9)	0.02
High blood pressure + High hematocrit	288	16	36.0 (4.43-292)	<0.01

- **Normal blood pressure** : Optimal + Normal
- **High blood pressure** : High normal + Hypertension
- **Low hematocrit** : first- third quartiles (<42.7%)
- **High hematocrit** : fourth quartile (≥42.7%)

•OR, odds ratio; CI, confidence interval

Discussion

1. **In the present study, we investigated the prevalence of RVO and its relevant risk factors in a general Japanese population. The results showed that the prevalence of RVO was 2.1%, and that age, high blood pressure, and elevation of hematocrit levels were independent risk factors for RVO.**

2. **Several previous population-based studies have also estimated the prevalence of RVO. The disease prevalence was reported as 1.6% in the Blue Mountains Eye Study in Australia and 1.1% in the Multiethnic Study of Atherosclerosis in the US. A study on a Chinese population, the Beijing Eye Study, reported an RVO prevalence of 1.2%, and a study on a Malay population, the Singapore Malay Eye Study, reported a prevalence of 0.7%. The prevalence of RVO in the present study (2.1%) thus seemed to be somewhat higher than those reported in previous studies. Our findings of a higher prevalence suggests that RVO is more common among the Japanese population than among Western populations and other Asians, since most of the above studies used the same grading protocols and RVO definitions.**

Discussion

3. **Our data indicated a clear association of hypertension with RVO, which is consistent with clinical knowledge and the findings of other population-based studies. In addition, our results also showed that not only hypertension but also high-normal blood pressure was significantly associated with RVO. Therefore, subjects with high-normal blood pressure should be considered a high-risk population for RVO. Strict control of elevated blood pressure may be important in preventing the disease.**

4. **We found that a higher hematocrit level was associated with RVO, independent of age, sex, and hypertension. A previous case-control study also indicated that hematocrit was significantly higher in RVO group than controls. RVO is caused by thrombosis of the vein, but the role played by various hematologic abnormalities in its etiology and pathogenesis still remains unclear and controversial. It is known that elevated hematocrit increases blood viscosity. Therefore, increased hematocrit may augment the risk of RVO through the increase in blood viscosity.**

Discussion

5. **The current study showed an extremely increased risk of RVO in subjects who had both hypertension and a higher hematocrit level. Although the mechanism underlying this phenomenon is not clearly understood, one possible explanation is that hypertension is a strong risk factor for systemic arteriosclerosis, including retinal arteriosclerosis, and sclerotic arteriolar walls in retina 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. It is, therefore, speculated that increased hematocrit levels markedly enhance the risk of RVO by hyperviscosity in people whose retinal vessel walls have already been damaged by hypertension.**

6. **This study has several limitations. First, we ascertained RVO cases by using one photographic field per eye, while in most previous population-based studies, 2-6 photographic fields were taken per eye. This could have resulted in underestimation of the prevalence of RVO if peripheral lesions were overlooked. Second, because of the cross-sectional design of this study, it is still unclear how risk factors are related to the onset of RVO. Further prospective investigation would help to clarify this issue.**

Conclusion

The results of this study suggest that RVO is more common among the Japanese then in Caucasians and other Asians, and that older age, higher hematocrit, and not only hypertension but also high-normal blood pressure are risk factors for RVO in the Japanese.

In addition, among subjects who have both high blood pressure and higher hematocrit, the risk of RVO was extremely increased. Therefore, subjects who have both high blood pressure and higher hematocrit should be considered a high-risk population of RVO, and will require continued preventive efforts to reduce the burden of the disease.

The 9-year incidence and risk factors for age-related macular degeneration in a general Japanese population : The Hisayama Study

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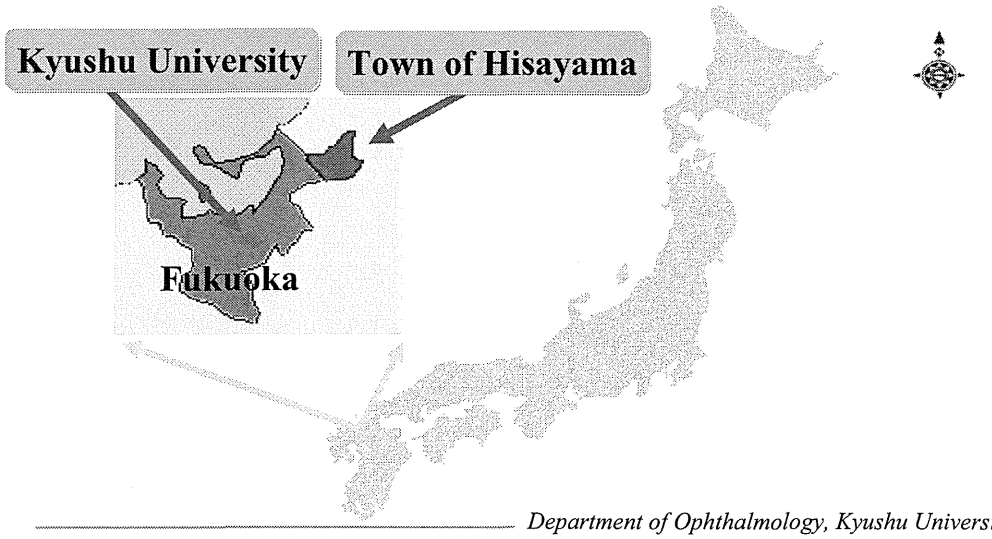
The Hisayama Study

The Hisayama Study is a long-term cohort study.
It has been conducted in the town of Hisayama since 1961.



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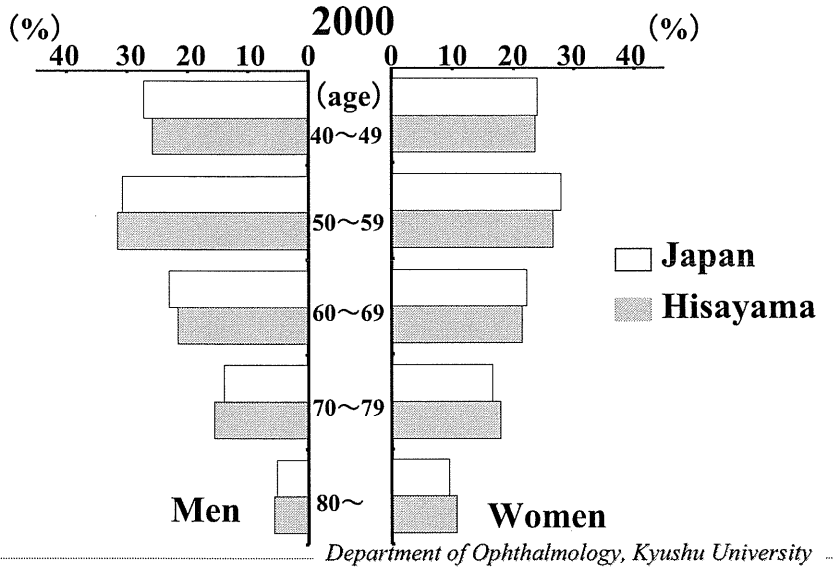
The Hisayama Study

The age distributions of Hisayama



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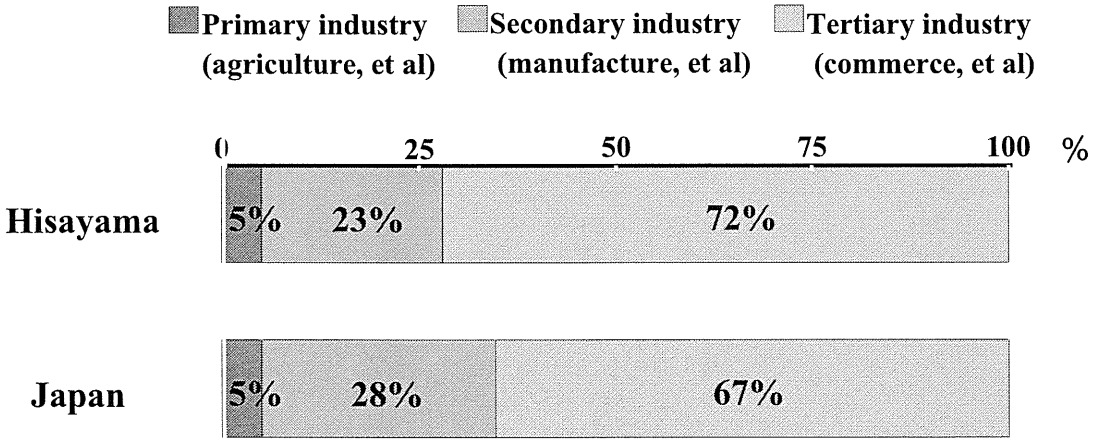
The Hisayama Study

The occupational distributions of Hisayama



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Purpose

1. **To estimate the 9-year incidence of early and late age-related macular degeneration (AMD) in a general Japanese population.**

2. **To examine the risk factors for the development of late AMD in Japanese.**

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Study Population

The target population of this study was all the residents aged 40 years and older.

Year		No. of the Study Subjects	
1998	---	1,775	(participation rate 43 %)
		↓	
2007	---	1,401	(follow-up rate 79 %)

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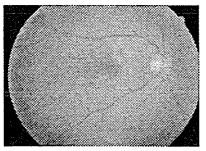
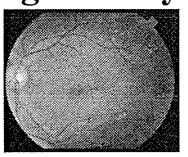
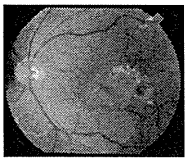
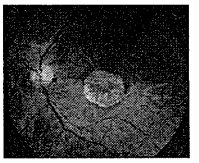
Methods : Definition of AMD

1. **Both examinations used a similar photographic grading technique based on the International Age-related Maculopathy Epidemiological Study Group grading protocol.**
   (Bird AC, et al. Surv Ophthalmol 39:367-374,1995)

2. **This protocol divides AMD into early and late stages.**
   - **Early stage : drusen or retinal pigmentary abnormalities**

   - **Late stage : neovascular AMD or geographic atrophy**

Methods : Statistical methods

1. **We calculated the age-adjusted incidence of AMD.**
   Age-adjusted incidences of AMD were calculated by means of the direct method using the World Health Organization standard population in 1998.

2. **We examined the relationship between risk factors and the development of late AMD.**
   We also estimated the age-adjusted and multivariate odds ratio and 95% confidence interval of each risk factor using a logistic regression analysis.

Methods : Risk factors

We considered the following nine risk factors for AMD.

- Age
- Sex
- Hypertension
- Diabetes
- Hyperlipidaemia
- Smoking habits
- Alcohol intake
- Body mass index (BMI)
- White blood cell (WBC)

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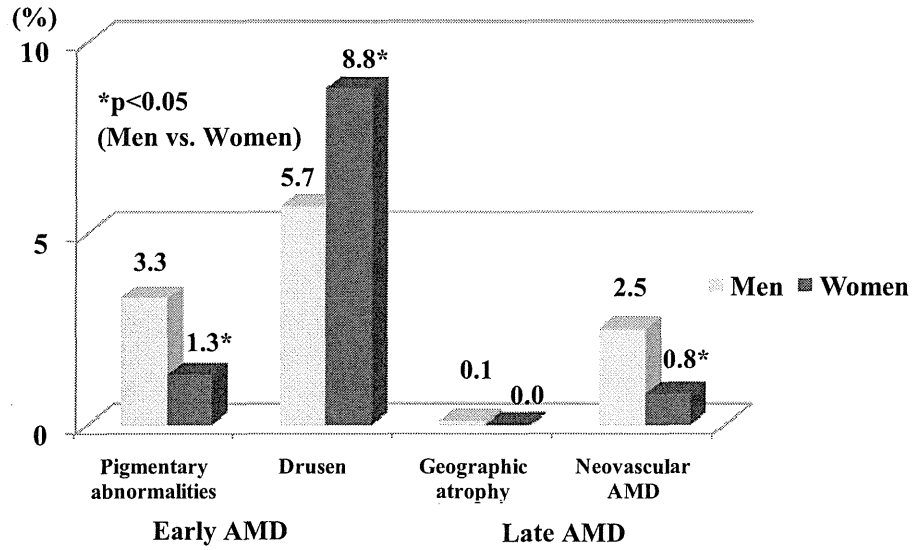
Results

Age-adjusted 9-year incidence of early and late AMD by sex, the Hisayama Study, 1998-2007



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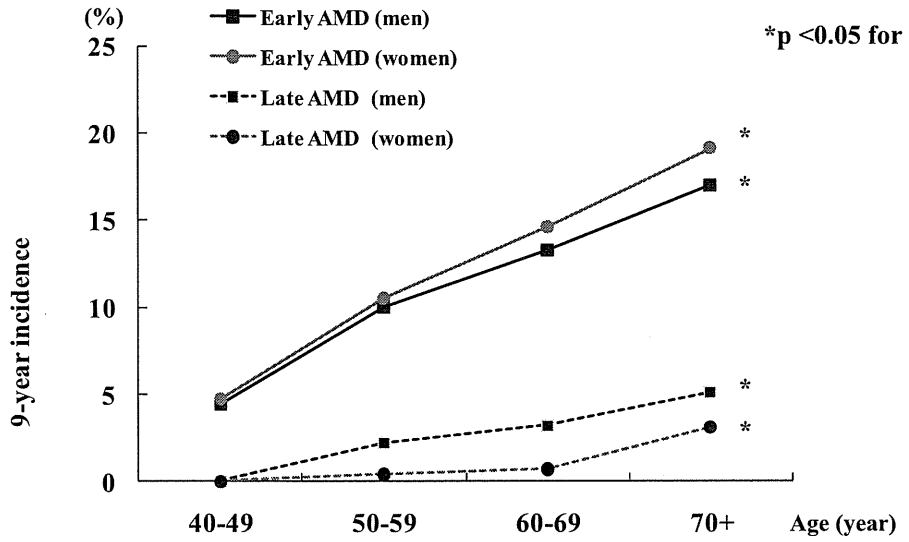
Results

Age-specific 9-year incidence of early and late AMD by sex, the Hisayama Study, 1998-2007



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Results

Total 9-year incidence of early and late AMD by sex, the Hisayama Study, 1998-2007

	incidence (%)		
	Men	Women	Total
Early AMD	9.0	10.4	10.0
Late AMD	2.6	0.8*	1.4

age-adjusted odds ratio =2.97
(95% confidence interval: 1.25-7.09, *p<0.05)

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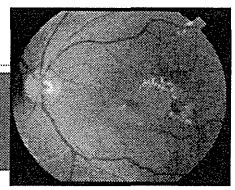
Results

The 9-year incidence of early and late AMD compared with other population studies

	Incidence (%)	
	Early AMD	Late AMD
The Blue Mountains Eye Study	12.7	3.3
The Beaver Dam Eye Study	10.9	1.9
The Barbados Eye Study	12.6	0.7
The Hisayama Study	10.0	1.4

Results

Age- and multivariate-adjusted odds ratios of risk factors for the development of late AMD



	Age-adjusted		Multivariate-adjusted	
Risk factor	OR	(95%CI)	OR	(95%CI)
Age (per 1 year)			1.10**	(1.05-1.16)
Sex (Men)	2.97*	(1.25-7.09)	0.86	(0.24-3.05)
Hypertension	0.79	(0.34-1.86)		
Diabetes	0.68	(0.16-1.23)		
Hyperlipidemia	1.39	(0.59-3.26)		
Smoking habits	4.59**	(1.86-11.3)	3.98*	(1.07-14.7)
Alcohol intake	1.88	(0.81-4.36)		
BMI (per 1 kg/m^2)	1.01	(0.88-1.15)		
WBC (per 10^3/mm^3)	1.52**	(1.19-1.95)	1.38*	(1.07-1.79)

OR: odds ratio, CI: confidence interval, **p<0.01, *p<0.05

Conclusions

1. **Late AMD is less common among the Japanese compared with white people in Western countries, while it is more common compared with black people. Racial difference in AMD incidence could be due to the difference in ocular pigmentation, or perhaps to genetic factors.**

2. **We found a significantly higher incidence of late AMD in men than in women. The reason for difference is unknown, but smoking habits might contribute to higher incidence of late AMD in Japanese men.**

Conclusions

3. **Smoking habits is relevant risk factor for late AMD in Japanese. As smoking is a well-recognized modifiable risk factor for AMD, therefore smoking cessation is important to reduce the burden of AMD, particularly among Japanese men.**

4. **Higher WBC is also relevant risk factor for late AMD in Japanese. This finding provides important epidemiologic evidence of an essential link between inflammation and late AMD development.**

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第48回日本網膜硝子体学会総会
第26回日本眼循環学会

生活習慣と糖尿病網膜症
:久山町研究

○安田美穂　畑快右　荒川聡　朝隈　朋子　石橋達朗
（九州大学眼科）
清原　裕（九州大学環境医学）

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喫煙

喫煙と増殖糖尿病網膜症には有意な関連がある

(Paetkau ME, *et al.* Lancet 2:1098-9, 1978)

喫煙と網膜症の発症、進展と関連を認めない

(Moss SE, *et al.* Ophthalmology 103:1438-42, 1996)

飲酒

飲酒と増殖糖尿病網膜症には有意な逆の関連がある

(Moss SE, *et al.* Ophthalmology 99:926-32, 1996)

飲酒と網膜症の発症、進展と関連を認めない

(Mckay R, *et al.* Br J Ophthalmol 84:865-70, 2000)

運動

余暇時の運動時間が長いほど血糖コントロールが良い

(Waden J, *et al.* Diabetes care 28:777-82, 2005)