

Paper published in *Investigative Ophthalmology and Visual Science*[§]

“Is the Association between Smoking and the Retinal Venular Diameter Reversible following Smoking Cessation?”

Masahide Yanagi, Munechika Misumi, Ryo Kawasaki, Ikuno Takahashi, Katsumasa Itakura, Saeko Fujiwara, Masazumi Akahoshi, Kazuo Neriishi, Tien Yin Wong, Yoshiaki Kiuchi
Invest Ophthalmol Vis Sci 2014 (January); 55(1):405–11 (doi:10.1167/iovs.13-12512)

Study Findings

After adjustment for such related factors as age, sex, blood pressure, body mass index (BMI), lipid profile, and radiation dose, this analysis of female A-bomb survivors showed that (1) the caliber of veins in the retina increases with the number of cigarettes smoked, and that (2) vein (venular) caliber differences between former smokers and those who never smoked diminished, until 10 years after quitting smoking their calibers were nearly identical.

Explanation

Smoking has long been considered a risk factor for circulatory diseases (hypertension, myocardial infarction, and stroke), and it may have harmful effects on the structure of blood vessels. Retinal vessel caliber, measured from digital images of the fundus, is considered a good indicator of blood vessel structure, and such changes have been reported to be associated with smoking in various epidemiological studies. However, there has been little or no data regarding whether the association increases with the number of cigarettes smoked, and whether there also are changes in retinal vessel caliber among people who have stopped smoking. This epidemiological study addresses those gaps in our knowledge about smoking and blood vessel caliber.

1. Objectives

To elucidate the association between habitual smoking or smoking cessation and retinal vessel caliber changes among A-bomb survivors in Hiroshima and Nagasaki who have been followed by the Radiation Effects Research Foundation through biennial health examinations (Adult Health Study: AHS).

2. Methods

Digital images of the fundus/retina were made for 1,664 participants in AHS ophthalmological examinations from 2006 to 2008. To observe retinal vessel caliber, standard indices, called the central retinal artery and vein equivalents (CRAE and CRVE), were calculated using image analysis software. To assess smoking habits, current smoking status was confirmed based on AHS medical history records, and the average number of cigarettes smoked per day was calculated. Information about smoking cessation was confirmed based on past AHS medical history records and mail survey information, and the number of years of smoking

cessation was calculated. Allowing for related factors such as age, sex, blood pressure, BMI, lipid profile, diabetes, C-reactive protein, white blood cell count, and radiation dose, the association between habitual smoking or smoking cessation and changes in retinal vessel (artery/vein) caliber was evaluated.

3. Results

- (1) CRAE: No significant association was observed between habitual smoking or the number of years of smoking cessation and retinal artery caliber in either males or females.
- (2) CRVE: Retinal venular caliber was positively associated with the number of cigarettes smoked per day among female smokers. Compared with non-smokers, CRVE was increased by about 5% on average for those who smoked 10 or more cigarettes per day (trend $p = 0.001$). Among females, while the retinal venular caliber of those who had stopped smoking for less than 10 years was significantly larger than that of non-smokers, the venular caliber for never smokers and those who had stopped smoking for 10 or more years was indistinguishable ($p = 0.99$). No significant associations of either retinal artery or venular calibers were observed among males for smoking frequency or the number of years of smoking cessation.

4. Discussion

1) The results of this study, which find that retinal venular caliber is significantly associated with habitual smoking and the number of years of smoking cessation, are similar to those of several other epidemiological studies, such as the Rotterdam Study and the Singapore/Malay Study. Increased venular caliber is generally believed to be associated with circulatory diseases (e.g., cerebral ischemia). Smoking is known to accelerate both inflammation and vascular endothelial dysfunction. Yet in this study an analysis adjusting for the effects of typical inflammation markers (white blood cell count and C-reactive protein) still showed an association between smoking and retinal venular caliber, which suggests there may be non-inflammation-mediated effects on blood vessels as a result of smoking.

2) Generally, aging effects on the blood vessels appear earlier in males than in females. In this study, smoking effects were not observed in males. A possible reason for this is that men tend to experience accelerated effects of aging on the blood vessels, such as hardening of vessel walls, which may have masked smoking effects on the vessels among our study cohort at the time of examination (average age: 73.8).

3) The results of this study suggest that among Japanese females smoking cessation for a sufficient period of time may reverse the effects of smoking on retinal venular caliber. These results also shed some mechanistic light on the various reports that 10 or more years of smoking cessation decrease the risk of mortality from myocardial infarction and cerebral infarction.

The Radiation Effects Research Foundation has studied A-bomb survivors and their offspring in Hiroshima and Nagasaki for more than 60 years. RERF's research achievements are considered the

principal scientific basis for radiation risk assessment by the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) and for recommendations regarding radiation protection standards by the International Commission on Radiological Protection (ICRP). RERF expresses its profound gratitude to the A-bomb survivors and survivors' offspring for their cooperation in our studies.

§ *Investigative Ophthalmology and Visual Science (IOVS)*, published online several times a month, is an official journal of the Association for Research in Vision and Ophthalmology (ARVO), an international organization whose purposes are to encourage and assist research, training, publication, and dissemination of knowledge in vision and ophthalmology. Included are original contributions that emphasize clinical and laboratory hypothesis-based research with statistically good results that clearly advance the fields of ophthalmic and vision research. (2012 impact factor for *IOVS*: 3.441)