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Letters to the Editor

Incidence of retinal artery occlusion in Germany

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Dear Editor,

Retinal artery occlusion (RAO) is a rare and severe disease potentially causing blindness. New therapeutic options such as systemic lysis are being evaluated (Schrag et al. 2015). Subjects with retinal arteriolar emboli are at increased risk of stroke (Wong & Klein 2002; Hayreh 2011) and giant cell arteritis and need prompt diagnostic assessment and treatment. Literature on incidence is scarce, with one report of annual incidence of 1.3/100 000 subjects for central RAO available for the USA (Leavitt et al. 2011). There is no data yet available for Europe (Li et al. 2017), a research gap we fill herein.

Based on health claims data of the 'AOK Baden-Wuerttemberg' (AOK BW) from 2013 to 2017, a secondary data analysis was carried out under fulfilment of data protection laws. The 'AOK BW' insures more than 40 % (n = 4 104 201) of subjects living in Baden-Württemberg, Germany. The study is based on pseudonymized administrative claims data. Thus, no ethical approval was needed.

Medical individual-level data are collected quarterly for each year. The collected data cover demographic data, inpatient and outpatient diagnosis data, which are coded according to the International Classification of Diseases 10th revision German Modification (ICD-10 GM).

The study population for prevalence estimation was defined as all insured persons of the AOK BW. Prevalent cases were defined as those subjects with RAO codes (ICD-10 code H34.1-2) in 2016, either in an outpatient setting by an ophthalmologist in one quarter of the year and confirmed in one of the following three quarters or coded at least once as inpatient.

All persons being continuously insured at the AOK BW from 01.01.2014 to 31.12.2017 were included in the incidence analysis. Those subjects with no RAO codes (ICD-10 code H34.1-2) in 2014 and 2015 were included in the analysis sample. Incident cases were defined corresponding to prevalent cases (outpatient diagnosis in two different quarters or one inpatient diagnosis) as outlined above. Stratification by type of RAO (central RAO: ICD-10 code H34.1; other RAO: ICD-10 code H34.2) was conducted. All analyses were performed with Structured Query Language (Oracle, Redwood Shores, CA, USA). Age and sex standardization according to the European standard population from 1976 was performed.

The crude prevalence in 2016 for central RAO was 12.5/100 000 person-years (py) and standardized prevalence 6.2/100 000 py, as well as 20.2/100 000 py and 11.7/100 000 py for other RAO, respectively. A total of 3 262 617 subjects were included in the incidence analysis. The crude incidence rate for central RAO was 5.8/100 000 py (standardized incidence rate: 2.7/100 000 py) and for other RAO 7.8/100 000 py (standardized incidence rate: 4.5/100 000 py). There is an increase with age: while under the age of 60 years, there is rarely any case of RAO, the incidence increases up to 57.0/100 000 py at the age of 80 to 84 years (Figure 1).

Using health claims data comes with several limitations including misclassification and under/over-reporting. We therefore only included outpatient data from ophthalmologists. In summary, we report incidence of RAO in Germany for the first time using health claims data and found it to be slightly higher than the data for the US (Leavitt et al. 2011).

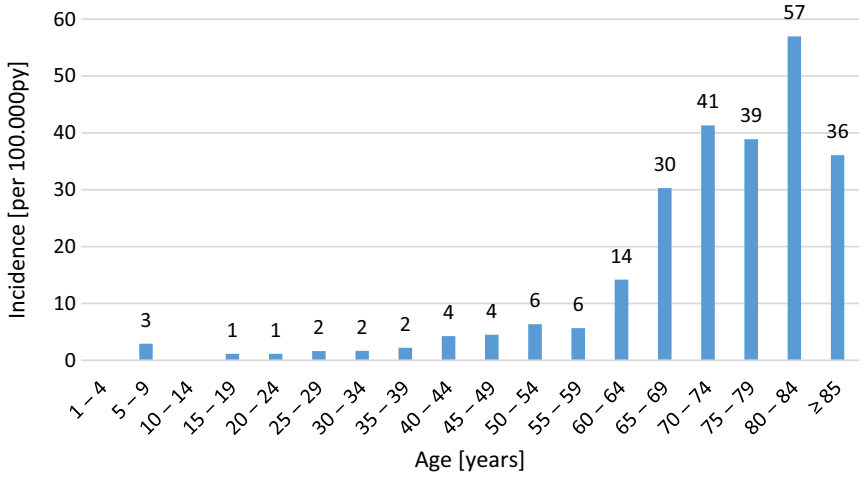

Fig. 1. Incidence of retinal artery occlusion (ICD-10 H34.1-2) stratified by age. Data from the health insurance AOK Baden-Württemberg in Germany in 2016.

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Longitudinal seasonal variations of intraocular pressure in primary open-angle glaucoma patients as revealed by real-world data

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Editor,

Elevated intraocular pressure (IOP) is one of the primary risk factors for glaucoma, a very common yet devastating group of eye diseases that often lead to blindness. Therefore, it is vital to monitor and control a patient's IOP to prevent the progression of the disease (Heijl et al. 2002). In this study, we analysed our real-world data of IOP derived from primary open-angle glaucoma (POAG) patients over a 20-year period to evaluate the long-term trend of IOP in patients treated at specialized clinics in Japan.

This study was approved by the Institutional Review Board of Kyoto Prefectural University of Medicine (KPUM), Kyoto, Japan. We analysed the real-world data of IOP comprised of 80 258 independent data points derived from 2781 POAG patients (1186 males and 1595 females; mean age: 60.8 ± 14.1 years) who were prescribed anti-glaucoma medications and underwent multiple follow-up examinations over a 20-year period (mean follow-up period: 5.5 ± 4.7 years) at the KPUM University Hospital, the Baptist Eye Clinic, or the Oike-Ikeda Eye Clinic. The IOP data were extracted from our clinical database, first established in 1995, that currently consists of more than 200 000 data points comprised of several clinical measurements under the following conditions: (1) 1 data point per patient per month, (2) if bilateral data were available, the right-eye data were used, (3) if measured more than twice within 1 month, the mean IOP data were calculated and used, and (4) if the patient received glaucoma surgery, the postoperative data were excluded. The mean IOP from all available data at each month from January 1997 through December 2016 was then calculated.

The seasonal variations were analysed via the following regression model formula (Gamus et al. 1995): $Y_{IOP} = \alpha\cos\{2\pi(X_{month} - X_{offset})/12\} + \beta X_{month} + \gamma$, where (1) Y_{IOP} represents the mean IOP of POAG patients, (2) X_{month} was coded as 1 (January 1997) through 240 (December 2016), (3) X_{offset} represents the month when the IOP reaches maximum, which was coded as 2 in this study, (4) α represents the amplitude of IOP, (5) β represents the slope of long-term IOP reduction, and (6) γ represents the intercept. If α differed significantly from 0, it was regarded as that a seasonal pattern of IOP through the year was observed.

The monthly average ambient temperature of the city of Kyoto from 2009 to 2016 was extracted from the database provided by the Japan Meteorological Agency (http://www.jma.go.jp/jma/index.html).

Our results showed a continuous decrease of IOP ($\beta = -0.016$, $p < 0.05$), suggesting that the management of IOP has been successfully controlled in Japan, owing to the effective anti-glaucoma medication prescribed by the glaucoma specialists. Surprisingly, the IOP decrease was accompanied by distinct seasonal variations (Bengtsson 1972; Gamus et al. 1995), that is annual elevation of IOP in winter and decrease of IOP in summer ($\alpha = 0.542$, $p < 0.05$), throughout the 20-year data period (Fig. 1A). The seasonal variation of IOP was clearly, yet inversely, correlated with the ambient temperature in the city of Kyoto, probably due to the response of the sympathetic nervous system to the ambient temperature (Fig. 1B).

Living organisms reportedly possess natural physiological processes known as 'circannual rhythms' (Küller 2002; West & Wood 2018) for adaptation to seasonal changes in response to environmental factors, such as temperature and day length (i.e. photoperiod/light–dark cycle). Our real-world data obtained from POAG patients in Kyoto, which is geographically located in the centre of Japan and has four distinct seasons, clearly showed that a circannual rhythm of IOP exists in the microenvironment of the eye tissue in local area residents, even under the pathophysiology of POAG, and revealed longitudinal seasonal variations of IOP for 20 consecutive years.

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