Common eye diseases in older adults of southern Germany: results from the KORA-Age study

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Purpose: a population-based study in the region of Augsburg (Germany, KORA) was used to identify the prevalence of eye diseases and their risk factors in a sample of aged individuals.

Methods: data originated from the KORA-Age study collected in 2012 and 822 participants (49.6% women, 50.4% men, aged 68–96 years) were asked standardised questions about eye diseases. Positive answers were validated and specified by treating ophthalmologists. Additional information came from laboratory data. Polymorphic markers were tested for candidate genes.

Results: we received validations and specifications for 339 participants. The most frequent eye diseases were cataracts (299 cases, 36%), dry eyes (120 cases, 15%), glaucoma (72 cases, 9%) and age-related macular degeneration (AMD) (68 cases, 8%). Almost all participants suffering from glaucoma or from AMD also had cataracts. Cataract surgery was associated with diabetes (in men; OR = 2.24; 95% confidence interval [CI] 1.11–4.53; P = 0.025) and smoking (in women; OR = 6.77; CI 1.62–28.35; P = 0.009). In men, treatments in airway diseases was associated with cataracts (glucocorticoids: OR = 5.29, CI 1.20–23.37; P = 0.028; sympathomimetics: OR = 4.57, CI 1.39–15.00; P = 0.012). Polymorphisms in two genes were associated with AMD (ARMS2: OR = 2.28, CI 1.48–3.51; P = 0.005; CFH: OR = 2.03, CI 1.35–3.06; P = 0.010).
Conclusion: combinations of eye diseases were frequent at old age. The importance of classical risk factors like diabetes, hypertension and airway diseases decreased either due to a survivor bias leaving healthier survivors in the older age group, or due to an increased influence of other up to now unknown risk factors.

Keywords: older people, population study, ageing, cataract, AMD, glaucoma

Introduction

More than any other species, humans are dependent on their vision for social interactions. Therefore, correct vision is one of the most prominent factors of quality of life. However, visual impairment is one of the leading disorders in older adults affecting 246 million people worldwide and an additional 39 million people are blind. Globally, the major causes of visual impairment are refractive errors (43%), unoperated cataract (33%) and glaucoma (2%). 65% of all people suffering from visual impairment are aged 50 and older [1]. The global causes of blindness are cataract (51%), glaucoma (8%), age-related macula degeneration (AMD) (5%), childhood blindness and corneal opacities (each 4%), uncorrected refractive errors and trachoma (each 3%), diabetic retinopathy (1%) and undetermined causes (21%) [1]. Visual impairment of the aged population is one of the main causes of diminished independence, mobility restriction, falls and fractures [2, 3].

Besides being the most frequent eye disease, cataracts show various degrees of prevalence in different ethnic groups as outlined by several population-based studies. Moreover, cataracts are also discussed as an independent marker of early mortality [4]. Obviously, this is particularly true for nuclear or mixed cataracts. More recently, a meta-analysis of 10 population-based studies was published [5] indicating that the presence of any cataract was significantly associated with a higher risk of death (hazard ratio 1.43; 95% confidence interval 1.21–2.02; P < 0.001). However, it remains an open question whether cataract formation is a consequence of co-morbidities (like diabetes), of environmental factors (like UV-light or nutrition) or of genetic influences.

Similar questions have been raised also for the age-related macular degeneration (AMD), however with a different outcome: African Americans and Caribbeans have a higher frequency of cataracts than people of European origin [4], but in contrast, AMD has a higher prevalence in people of European ancestry compared with Hispanics, Asians and people of African ancestry [6]. Besides these differences in ethnic association, association with diabetes is frequently being reported for (late) AMD, too [7].

For Europe, a recent literature review was published on the prevalence of major eye diseases [4] focusing on AMD, glaucoma and diabetic retinopathy in general populations. The prevalence data given for AMD in individuals aged 65–75 years are 9–25%. Diabetic retinopathy affects 3–4% of the overall European population, but for individuals over 60 years of age it varies between 11% in Germany and 17% in France. For glaucoma, it varies between 3% in France and 14% in Germany [8].

For Southern Germany, we recently evaluated the prevalence of major eye diseases and co-morbidities in the population-based KORA-F4 study (Cooperative Health Research in the Region of Augsburg [Germany]) [9]. In this study, almost 2600 participants 32–71 years of age were asked in a questionnaire for the presence of cataracts, glaucoma and retinal disorders. Positive answers were validated and specified by treating ophthalmologists. We revealed a similar profile of major risk factors for cataracts (age, female sex and diabetes) [9] as described in other international studies [10–12].

As the unique feature of this study, we present here data of a cross-sectional study on older participants (aged 68–96 years). The objective of our study was to examine prevalences, co-morbidities and risk factors of eye diseases in the aged. Specifically, we wanted to show that the prevalence of the most relevant eye diseases increases in the higher age groups even stronger than at younger age indicating specific risk profiles for co-morbidity patterns and associated medication. Along this line, we tested whether eye diseases in older participants are associated with lifestyle parameters (smoking and alcohol consumption) and protective and risk alleles for eye diseases.

Methods

The population-based KORA-Age study was conducted in the region of Augsburg, Southern Germany [13]. An age- and sex-stratified sample of participants of the previous four cross-sectional surveys S1–S4 (1984–2000) [14] born before 1944 was invited to participate in an examination in 2009 (KORA-Age1) and was re-invited 3 years later for a follow-up. In 2012, 822 participants between 68 and 96 years of age completed re-examination (named KORA Age2) [15]. Since the previously reported F4 analysis [9] contributed only partly to Age2, Age2 could not be designed as follow-up (see Supplementary Figure S1, available at Age and Ageing online).

KORA-Age2 was carried out in accordance with the Declaration of Helsinki, including written informed consent of all participants and to contact the treating ophthalmologists. All study methods were approved by the ethics committee of the Bavarian Medical Association.

For the detailed description of the methods [estimation of eye disorders, assessment of co-variables, statistics and...
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Table 1. Sub-classification of eye disorders by ophthalmologists.

| Eye disease               | Number of cases* |
|---------------------------|------------------|
| Corneal diseases          | 129 (16%)        |
| Dry eye                   | 120              |
| Corneal opacification     | 38               |
| Cataracts                 | 299 (36%)        |
| Nuclear cataract only     | 77               |
| Cortical cataract only    | 76               |
| Nuclear and cortical cataract | 38         |
| Posterior cataract only   | 20               |
| Subcapsular cataract only | 9                |
| Posterior and subcapsular cataract | 0 |
| No detailed diagnosis given | 76             |
| Cataract extraction       | 190              |
| Glaucoma                  | 72 (9%)          |
| Open-angle glaucoma       | 53               |
| Optic nerve excavation    | 35               |
| Visual field anomalies    | 25               |
| Closed-angle glaucoma     | 6                |
| Retinal disorders         | 110 (14%)        |
| AMD                       | 68               |
| Macula oedema             | 9                |
| Thrombosis                | 9                |
| Gliosis of the macula     | 6                |
| Vessel anomaly            | 5                |
| Diabetic retinopathy      | 5                |
| Tumour                    | 2                |
| Retinitis pigmentosa      | 1                |
| Retinoschisis             | 1                |

*Combined diagnoses are possible; percentage is given for the entire cohort (n = 822).

We represented 63% of the overall cataracts. There is no sex effect (P = 0.155); in 59% of the cataractous males and in 67% of the cataractous women cataracts have been extracted.

The age-dependent increase of the prevalence of major eye diseases, dry eyes, cataracts, glaucoma and AMD is given in Supplementary Figure S2, available at Age and Ageing online. The risk of dry eyes increased with age (P = 0.013), and women had a higher risk for dry eyes than men [odds ratio = 1.89 (1.28–2.79), P = 0.001]. For cataracts, we observed a highly significant association between increasing age and the frequency of cataracts (P < 0.001) with female sex as a relevant risk factor [odds ratio for women versus men = 1.76 (1.28–2.41), P < 0.001]. Among the 72 validated cases of glaucoma, most were open-angle glaucoma (74% of all glaucoma cases). With age, the risk of glaucoma increased (P = 0.004), but we did not observe any sex difference (P = 0.443). Among the 68 cases of AMD, we observed similarly an increasing risk with age (P < 0.001) and no sex effect (P = 0.610).

In analysing co-morbidity of eye diseases (Table 2) with diabetes, hypertension and airway diseases, we identified a significant association of diabetes with cataract surgery in men. Similarly, sympathomimetic drugs or inhaled glucocorticoids (used in the treatment of chronic airway diseases) were highly significant risk factors for cataracts in older men. Other eye disorders did not show co-morbidity with diabetes, hypertension and airway diseases, even if different subgroups of eye diseases (Table 1) were analysed.

Statistically significant findings among lifestyle and laboratory data are summarised also in Table 2. We identified alcohol and actual smoking only in older women as a risk factor for glaucoma or cataract surgery, respectively. Thyroid hormone replacement therapy in women was a risk factor for dry-eye syndrome, but was inversely associated with AMD. Males treated with thyroid hormones had a

Figure 1. Overlapping prevalence of the three major eye diseases (validated cases only).
significantly higher risk for glaucoma. Among metabolites and enzyme activities, uric acid and alkaline phosphatase activity appear to have protective effects in women only: alkaline phosphatase for dry eye syndrome and uric acid for cataracts in general.

We investigated a limited number of candidate genes (see Supplementary Table S1, available at Age and Ageing online) for their association with eye disorders. Due to low minor allele frequencies and the low sample size of KORA, we had limited power to detect significant associations for AMD and glaucoma. Nevertheless, two SNPs (rs1049024 within the ARMS2 gene [17], and the risk of sympathomimetic drugs or inhaled glucocorticoids for cataractogenesis is well known [18]). The preferred sequence of cataract formation followed by AMD is also in line with previous observations of an association of cataract surgery with late AMD [19]. On the other hand, the low frequency of diabetic retinopathy in our cohort of older people is surprising compared to previous studies [reviewed in 4]. It might be argued that most of the affected patients did not survive to become included into our cohort of older people, because these patients suffer from an increased burden of mortality due to complications of chronic hyperglycaemia, like renal failure and cardiovascular diseases [20].

Moreover, the significantly higher risk for glaucoma in males treated with thyroid hormones is consistent with the observation that hypothyroidism patients were found to have a greater risk of developing open-angle glaucoma than the control cohort [21]. Besides the different features of the various eye diseases, the sex-specific differences are also important to notice. These detailed aspects refine the previous knowledge of sex-dependent prevalence in age-related eye diseases that are discussed mainly in the context of hormonal changes in women over lifetime [22].

Concerning the association with genetic risk factors for age-related eye diseases, we observed only two SNPs (in the genes ARMS2 and CFH) being significantly associated with AMD. Among others, both are frequently found to be associated with AMD [23–27]. However, we could not confirm the protective and risk alleles for cataracts, which we have found previously for the younger KORA cohort [9].

The SNP in the ARMS2 gene leading to an A69S exchange is predicted to be probably damaging (PolyPhen-2, http://genetics.bwh.harvard.edu/pph2/, score of 0.994), since it introduces a Ser residue, which might be used as a new phosphorylation site (score of 0.905, NetPhos 2.0. http://www.cbs.dtu.dk/services/NetPhos/). The SNP in the CFH gene corresponds to the amino-acid exchange Tyr402His in the CFH gene, but the Tyr residue is most likely not used as a phosphorylation site (score 0.142, NetPhos 2.0).

Nevertheless, we are aware of the limits of our study design: in general, our findings of ocular disorders are restricted to clinically relevant cases, and less severe phenotypes may have remained in the controls. Since aged persons in Germany usually see an ophthalmologist routinely, such misclassification bias might be neglected in the higher age group. Moreover, the individual ophthalmologists might

Table 2. Association of major eye diseases with common illnesses, medication, laboratory data or lifestyle factors.

| Eye disease | Associated factor | OR  | CI lower | CI upper | P value |
|-------------|------------------|-----|----------|----------|---------|
| (a) in women |                  |     |          |          |         |
| Dry eye     | Alkaline phosphatase (µkat/l) | 0.39 | 0.17 | 0.86 | 0.019 |
| Dry eye     | Thyroid therapy (yes) | 1.77 | 1.05 | 2.98 | 0.033 |
| AMD         | Thyroid therapy (yes) | 0.35 | 0.14 | 0.87 | 0.023 |
| Glaucoma    | Alcohol (no) | 0.35 | 0.13 | 0.96 | 0.042 |
| Cataract    | Uric acid (mg/dl) | 0.74 | 0.60 | 0.91 | 0.005 |
| Cataract surgery | Alkaline phosphatase (µkat/l) | 0.33 | 0.15 | 0.75 | 0.008 |
| Cataract surgery | Actual smoker (yes) | 6.77 | 1.62 | 28.35 | 0.009 |
| (b) in men  |                  |     |          |          |         |
| Glaucoma    | Thyroid therapy (yes) | 3.06 | 1.25 | 7.49 | 0.015 |
| Cataract    | Haemoglobin (g/l) | 1.42 | 1.08 | 1.87 | 0.014 |
| Cataract    | Mean corpuscular haemoglobin (pg) | 0.24 | 0.08 | 0.76 | 0.015 |
| Cataract    | Erythrocytes (100,000 cells/µl) | 0.34 | 0.14 | 0.81 | 0.015 |
| Cataract    | Sympathomimetics (yes) | 4.57 | 1.39 | 15.00 | 0.012 |
| Cataract    | Glucocorticoids (yes) | 5.29 | 1.20 | 23.37 | 0.028 |
| Cataract surgery | Diabetes (yes) | 2.24 | 1.11 | 4.53 | 0.025 |

All models calculated are adjusted for age and gender.

Discussion

In this study, we could confirm diabetes (in men) and smoking (in women) as risk factors for cataract surgery and common SNPs in the genes ARMS2 and CFH for AMD. Moreover, many of our other findings are also in agreement with previous studies, e.g. our overall cataract prevalence is comparable to a recent population-based study in Finland [17], and the risk of sympathomimetic drugs or inhaled glucocorticoids for cataractogenesis is well known [18]. The preferred sequence of cataract formation followed by AMD is also in line with previous observations of an association of cataract surgery with late AMD [19]. On the other hand, the low frequency of diabetic retinopathy in our cohort of older people is surprising compared to previous studies [reviewed in 4]. It might be argued that most of the affected patients did not survive to become included into our cohort of older people, because these patients suffer from an increased burden of mortality due to complications of chronic hyperglycaemia, like renal failure and cardiovascular diseases [20].
use slightly different diagnostic criteria leading to a kind of uncertainty in the designation of the diseases. However, all diagnostic criteria have to fulfill the requirements of the German health-care insurances resulting in an intrinsic standardisation of our study.

Since association of age-related eye disorders with common diseases or lifestyle factors could be found only for cataract surgery, one might argue it is due to a survivor bias wherein severe diabetes leads to early mortality leaving only healthier survivors in the older age group [28]. This argument might hold true also for all other risk estimates and for other eye diseases.

As in our previous study [9], the main strength of this study is that self-reported eye diseases were validated and specified by treating ophthalmologists that allows a more detailed analysis than non-validated studies [16]. Moreover, there are two important aspects raised by this study in older participants that are different to previous studies. First, in older participants combinations of eye diseases are more frequent than in the younger cohorts. This makes the isolated consideration of particular eye disorders unhelpful for the therapy of older patients. Therefore, an integrated point of view might be rather appropriate. Second, the impact of classical risk factors like diabetes, hypertension and airway diseases decreases either due to a survivor bias leaving healthier survivors in the older age group, or due to an increased influence of other, up to now unknown, risk factors. If cataracts are the main entry point also for other eye diseases like AMD and glaucoma, the prevention of cataracts should get a very high priority.

**Key points**

- At older age, eye diseases affect ~50% of a population.
- At older age, combinations of eye diseases were more frequent than in younger people.
- At older age, the importance of classical risk factors for eye diseases (e.g. diabetes, hypertension, airway diseases) decreases.

**Supplementary data**

Supplementary data are available at Age and Aging online.

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A foodservice approach to enhance energy intake of elderly subacute patients: a pilot study to assess impact on patient outcomes and cost

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Abstract

Background: effective strategies are required to support the nutritional status of patients.
Objectives: to evaluate a foodservice nutrition intervention on a range of participant outcomes and estimate its cost.
Design: parallel controlled pilot study.
Setting: subacute hospital ward.
Subjects: all consecutively admitted adult patients were eligible for recruitment under waiver of consent.
Methods: the intervention was a modified hospital menu developed by substituting standard items with higher energy options. The control was the standard menu. All participants received usual multidisciplinary care. Outcomes were change in weight and hand grip strength (HGS) between admission and day 14 and; energy and protein intake and patient satisfaction with the foodservice at day 14. The additional cost of the intervention was also estimated.
Results: the median (interquartile range) age of participants (n = 122) was 83 (75–87) years and length of stay was 19 (11–32) days. One-third (38.5%) were malnourished at admission. There was no difference in mean (SD) HGS change (1.7 (5.1) versus 1.4 (5.8) kg, P = 0.798) or weight change (~0.55 (3.43) versus 0.26 (3.33) %, P = 0.338) between the intervention and control groups, respectively. The intervention group had significantly higher mean (SD) intake of energy (132