# Change of Intraocular Pressure Over 5 Years and its Relationship to Cardiovascular Parameters: Results From the Gutenberg Health Study

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**Purpose.** To investigate the longitudinal change in intraocular pressure (IOP) over 5 years and its relationship with cardiovascular parameters in a population-based sample in Germany.

**Methods.** The Gutenberg Health Study is a prospective, observational, single-center cohort study. The sample was equally stratified for sex, residence, and age decade. IOP was measured with noncontact tonometry at baseline and at 5-year follow-up. Cardiovascular parameters, including body mass index (BMI), systolic blood pressure, and diabetes status, were assessed. Participants without IOP measurement at one time point, who were taking IOP-lowering medications, or who had ophthalmic surgery during the 5-year follow-up interval were excluded, as well as those with glaucoma diagnosis. Univariable and multivariable linear regression analyses were conducted.

**Results.** This analysis included 9633 participants (48.9% female). The mean IOP increased from 14.04 ± 2.78 mmHg at baseline to 14.77 ± 2.92 mmHg at 5-year follow-up ($P < 0.001$). In multivariable linear regression analyses, an increase in BMI was associated with an increase in IOP over time ($P < 0.001$), whereas a higher baseline BMI was associated with a lower IOP change ($P < 0.001$). Higher age and male sex were associated with higher IOP change ($P < 0.001$). A change in systolic blood pressure was associated with IOP change, whereas baseline systolic blood pressure and diabetes status were not associated.

**Conclusions.** This population-based study found a relationship between IOP change over 5 years and BMI and systolic blood pressure change, respectively. These findings suggest the importance of monitoring cardiovascular risk factors in IOP management.

Keywords: intraocular pressure, blood pressure, body mass index, diabetes, epidemiology

Elevated intraocular pressure (IOP) is the leading and only therapeutically modifiable risk factor for the development and progression of glaucoma.[1,2] Cross-sectional studies have shown that cardiovascular parameters are further risk factors for open-angle glaucoma (OAG).[3,4] OAG diagnosis is associated with a lower body mass index (BMI),[5]

arterial hypertension,[6] and diabetes mellitus.[7] Similarly, IOP is associated with BMI, arterial hypertension, and diabetes.[8] In addition, IOP is also associated with waist-to-hip ratio,[9] but this has not been shown previously in OAG.[10] A positive association between BMI and IOP has been demonstrated in several cross-sectional studies[11] but is considered to be of minor importance clinically.[8] Baisakhiya et al.[9] demonstrated a correlation between higher IOP and waist-to-hip ratio, BMI, and obesity. The authors hypothesized that the association between obesity and increased IOP is caused by fat accumulation in the periorbital space, which leads to increased episcleral venous pressure.

Arterial hypertension is also positively associated with glaucoma.[12] The positive association between elevated blood pressure and IOP has been shown in multiple cross-section studies.[13,14] It is well known that glaucoma prevalence is higher in subjects with diabetes.[15] Whether there is an association between higher IOP and diabetes has been investigated in cross-sectional studies.[16]

The literature about differences in IOP between women and men is inconsistent. Some studies have demonstrated a higher IOP in women,[17] whereas other studies have found a significantly higher IOP in men[18] or no sex-related difference in IOP at all.[19]

Concerning aging, a relationship between older age and higher IOP[14] has been reported in some studies. In contrast, others have shown no association with age[20] or even a negative relationship between IOP and age.[21]

Longitudinal studies on IOP are rare but allow us to investigate IOP change over time with regard to age, sex, and changes in cardiovascular risk factors. Han et al.[22] reported longitudinal changes in IOP in a Chinese study cohort over 4 years (2010–2014). The average change in IOP was an increase of 0.43 mmHg, positively correlated with older age. Study participants with increased blood pressure or BMI had IOP elevation over time.

The Gutenberg Health Study (GHS) offers the opportunity to gain insights into the change of IOP and its relationship with cardiovascular parameters over time in a large and population-based European cohort. With one of the largest samples in which IOP is observed over time, it allows confirmation of previously reported cross-sectional findings in a longitudinal population-based study design.

## Methods

### Study Sample

The GHS is a population-based, prospective, observational, single-center cohort study in the Rhine-Main Region in Germany. The sample was equally stratified for sex, residence (urban or rural), and age decade. At baseline, 15,010 individuals were included (2007–2012), and 12,423 were re-examined after 5 years (2012–2017). Participants without IOP measurement at one time point, who were taking IOP-lowering medications, or who had ophthalmic surgery during the 5-year follow-up interval were excluded, as well as those with glaucoma diagnosis.

### Ophthalmic Parameters

During the initial examination, eye examinations were performed by medical staff. From the first follow-up at the study center, qualified study personnel took over this task. At both times, IOP was measured with noncontact tonometry and automatic air-puff control (NT 2000; Nidek Co., Tokyo, Japan). The mean of three measurements within a 3-mmHg range was obtained for each eye.[23] Most study participants were examined at a similar time at baseline and 5-year follow-up. In 98% of study participants, the time at follow-up examination did not differ by more than 2 hours from the time at the baseline examination. The time of year was also primarily consistent with baseline.

### Cardiovascular Parameters

Characteristics of the study population included age, sex, body height, and body weight. Anthropometric measurements were performed using calibrated digital scales (Seca 862; Seca, Hamburg, Germany), a Seca measuring stick, and a waist-measuring tape.[8] Diabetes mellitus was defined as an established physician diagnosis using antidiabetics or HbA1c $\geq$ 6.5%. Arterial hypertension was defined as the use of antihypertensive medication, a systolic blood pressure >140 mmHg (HEM-705CP *II*; Omron, Mannheim, Germany[24]), diastolic blood pressure > 90 mmHg, or an established medical diagnosis. Further information, such as HbA1c level, was determined by using standardized measurement procedures.

### Inclusion and Exclusion Criteria

For the selection of study participants, those without IOP measurement at one time point, who were taking IOP-lowering medications, or who had ophthalmic surgery during the 5-year follow-up interval were excluded (Supplementary Fig. S1).

### Statistical Analysis

Descriptive analysis was conducted for primary and secondary variables. For categorical parameters, absolute and relative frequencies were computed. For continuous variables, means and standard deviations were calculated for approximately normally distributed data; otherwise, median and interquartile range were calculated. IOP change was computed as the difference between the 5-year follow-up and baseline measurements for the identical eye. Pearson correlation analysis was conducted for the right eyes to analyze the association of IOP change and cardiovascular parameters. Multivariable linear regression analyses were conducted with generalized estimating equations on a person level to account for two eyes of one subject. First, univariable association analysis was computed adjusted for age and sex. Second, the cardiovascular factors were included in one multivariable model. If the baseline value and the 5-year change of a cardiovascular factor were significant, an additional model with an interaction term was planned to be included. Data were processed with R 4.0.3 (R Foundation for Statistical Computing, Vienna, Austria).

## Results

Overall, 9633 study participants were included. The mean age of the study population was 53.3 $\pm$ 10.5 years, and 48.9% were female. Table 1 shows the participants' characteristics at baseline; Supplementary Figure S1 shows the item non-responder analysis. The mean baseline IOPs in the right eye were 13.96 $\pm$ 2.96 mmHg in women and

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**Table 1.** Participants' Characteristics ($N = 9633$, Baseline Examination) and Cardiovascular Parameters in the Gutenberg Health Study

| | Overall | Men | Women |
|---|---|---|---|
| Anthropometric data (baseline) | | | |
| Participants, *n* | 9633 | 4921 | 4712 |
| Age (y), mean ± SD | 53.30 ± 10.5 | 53.58 ± 10.6 | 53.02 ± 10.4 |
| Age categories (y), mean ± SD | | | |
| 35–44 | 2378 ± 24.7 | 1.169 ± 23.8 | 1.209 ± 25.7 |
| 45–54 | 2891 ± 30.0 | 1.471 ± 29.9 | 1.420 ± 30.1 |
| 55–64 | 2610 ± 27.1 | 1.326 ± 26.9 | 1.284 ± 27.2 |
| 65–74 | 1754 ± 18.2 | 955 ± 19.4 | 799 ± 17.0 |
| Body weight (kg), mean ± SD | 79.34 ± 16.2 | 87.1 ± 14.0 | 71.3 ± 14.4 |
| Body height (cm), mean ± SD | 171 ± 9.5 | 177.5 ± 6.9 | 164.2 ± 6.6 |
| Cardiovascular parameters | | | |
| Arterial hypertension, *n* (%) | 4412 (45.8) | 2516 (51.1) | 1896 (40.2) |
| Diabetes, *n* (%) | 675 (7) | 436 (8.9) | 239 (5.1) |
| Change in diabetes over 5 years, % | | | |
| No diabetes | 88.5 | 87.0 | 92.1 |
| Newly diagnosed diabetes | 3.7 | 4.1 | 2.8 |
| Previous diabetes | 0.9 | 0.7 | 1.0 |
| Ongoing diabetes | 6.9 | 8.1 | 4.1 |
| HbA1c level, mean ± SD | 5.51 ± 0.63 | 5.55 ± 0.66 | 5.47 ± 0.59 |
| Systolic blood pressure (mmHg) , mean ± SD | 130.16 ± 16.85 | 133.0 ± 15.6 | 127.2 ± 17.6 |
| Diastolic blood pressure (mmHg) , mean ± SD | 82.31 ± 9.27 | 83.84 ± 9.15 | 80.7 ± 9.13 |
| Mean arterial pressure (mmHg), mean ± SD | 98.26 ± 10.92 | 100.23 ± 10.37 | 96.19 ± 11.09 |
| BMI (kg/m$^2$), mean ± SD | 27.06 ± 4.78 | 27.6 ± 4.1 | 26.5 ± 5.3 |
| Waist-to-hip ratio, mean ± SD | 0.92 ± 0.09 | 0.98 ± 0.07 | 0.86 ± 0.07 |
| Dyslipidemia, *n* (%) | 3091 (32.1) | 2030 (41.3) | 1061 (22.5) |
| Smoking, *n* (%) | 1803 (18.7) | 973 (19.8) | 830 (17.6) |
| Myocardial infarct, *n* (%) | 197 (2.0) | 154 (3.1) | 830 (17.6) |
| Arterial fibrillation, *n* (%) | 201 (2.1) | 138 (2.8) | 63 (1.3) |
| Chronic heart failure, *n* (%) | 78 (0.8) | 39 (0.8) | 39 (0.8) |
| Coronary disease, *n* (%) | 324 (3.4) | 257 (5.2) | 67 (1.4) |
| Peripheral disease, *n* (%) | 251 (2.6) | 141 (2.9) | 110 (2.3) |
| LDL/HDL ratio, mean ± SD | 2.58 ± 0.92 | 2.89 ± 0.92 | 2.25 ± 0.80 |
| Ophthalmic parameters | | | |
| IOP (mmHg), right eye, mean ± SD | 14.04 ± 2.78 | 14.10 ± 2.86 | 13.96 ± 2.69 |
| IOP (mmHg), left eye, mean ± SD | 14.19 ± 2.81 | 14.31 ± 2.89 | 14.06 ± 2.71 |
| Central corneal thickness (µm), right eye, mean ± SD | 552.04 ± 35.65 | 553.86 ± 35.42 | 550.14 ± 35.80 |
| Central corneal thickness (µm), left eye, mean ± SD | 555.64 ± 35.54 | 557.60 ± 35.46 | 553.59 ± 35.51 |

LDL, low-density lipoprotein; HDL, high-density lipoprotein.

**Table 2.** Changes in Ophthalmic and Cardiovascular Parameters Over 5 Years

| | Mean ± SD | | |
|---|---|---|---|
| | Baseline (2007–2012) | Follow-Up (2012–2017) | Change Over 5 Years |
| IOP (mmHg), right eye | 14.04 ± 2.78 | 14.77 ± 2.92 | 0.73 ± 2.04 |
| IOP (mmHg), left eye | 14.19 ± 2.81 | 14.85 ± 2.93 | 0.67 ± 2.04 |
| Systolic blood pressure (mmHg) | 130.16 ± 16.85 | 130.21 ± 16.51 | 0.05 ± 14.12 |
| Diastolic blood pressure (mmHg) | 82.31 ± 9.27 | 80.68 ± 9.31 | −1.63 ± 8.30 |
| BMI (kg/m$^2$) | 27.06 ± 4.78 | 27.44 ± 4.98 | 0.38 ± 1.74 |
| Waist-to-hip ratio | 0.92 ± 0.09 | 0.92 ± 0.09 | 0.00 ± 0.06 |
| HbA1c level (%) | 5.51 ± 0.63 | 5.64 ± 0.61 | 0.13 ± 0.46 |

14.10 ± 2.86 mmHg in men; at 5-year follow-up, they were 14.65 ± 2.79 mmHg in women and 14.87 ± 3.03 mmHg in men. IOP increased in the right eye by 0.73 mmHg over 5 years.

During the 5 years, mean arterial blood pressure increased by 0.73 mmHg in women and decreased by 0.60 mmHg in men. The average BMI also increased more in women (0.49 kg/m$^2$) than in men (0.29 kg/m$^2$), whereas the increase in blood glucose levels was similar between both (0.12% and 0.13%, respectively). However, there were slightly more new diabetes diagnoses in men (4.1%) than in women (2.8%) (Tables 1, 2).

Among the excluded participants, the average age was 5 years older. There was a low frequency of participants with hypertension and slightly fewer people with diabetes. The other cardiovascular parameters showed comparable results. The IOP values were higher in the group of excluded participants (Supplementary Table S1). The mean change in IOP over 5 years (mean follow-up time, 5.04 ± 0.25 years) was 0.73 ± 2.04 mmHg in the right eye. The change in IOP was

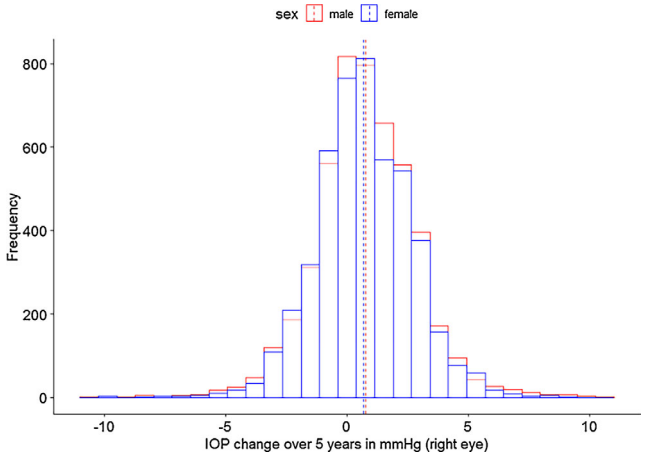


**Figure 1.** Distribution of IOP change over 5 years (right eye), based on the population-based Gutenberg Health Study ($N = 9590$ eyes; 2007–2017).

slightly higher in men (0.77 ± 2.11 mmHg) than in women (0.69 ± 1.96 mmHg; $P < 0.05$) (Fig. 1).

### Univariable Analysis

Change in IOP was associated with age ($P < 0.001$) (Fig. 2A). Men showed a higher IOP change over 5 years than women ($P = 0.04$). IOP at baseline and IOP change over 5 years were associated; if the baseline IOP value was higher, the IOP change over 5 years tended to be lower (Fig. 2B, Table 3). The other results of univariable analysis showed an association between IOP change with several cardiovascular parameters. The strongest association was found with the 5-year changes in systolic, diastolic, and mean arterial blood pressure (Figs. 2C–2H, Table 3).

The boxplots in Figure 3 show the changes in IOP stratified for diabetes status. For newly diagnosed diabetics, the median is slightly higher than in the other groups ($P = 0.70$). Univariable analysis correlated ongoing diabetes and IOP change ($P = 0.04$). However, no further graphical evidence exists that the IOP change is higher in any group. Looking at diabetes status and the corresponding IOP change stratified by sex, we found that the median was slightly higher among women in the previously diagnosed group. In contrast, the median was highest among men in the newly diagnosed group.

### Multivariable Regression Analysis

Associations between IOP change and baseline and change in cardiovascular risk factors were evaluated in multivariable linear regression analysis (Table 3). The average IOPs (baseline and follow-up) were included as a predictor variable because IOP change is connected to the IOP level. The goal was to make sure to observe correlations between IOP change and its relation to cardiovascular risk factors instead of looking at the IOP level and how it is connected to these risk factors. The results of the multivariable model were comparable to a model without IOP average as a predictor variable. Also, the regression analysis was performed including baseline IOP as predictor variable instead of IOP average; this analysis showed comparable results. Baseline BMI was negative, and changes in BMI over 5 years were positively associated with IOP changes. The baseline waist-to-hip ratio showed a positive association, but the 5-year change was not associated with IOP change. Systolic blood pressure was included in the regression model instead of diastolic blood pressure because systolic blood pressure showed a higher correlation with IOP change. This was also the case in other studies.[16] In addition, the pulse amplitude was included.

In multivariable regression analysis, a one-unit increase in BMI and a 10-mmHg increase in systolic blood pressure were associated with average increases in IOP of 0.07 mmHg and 0.02 mmHg, respectively. However, a higher baseline BMI was associated with a 0.03-mmHg lower IOP. Baseline pulse amplitude showed no significant association with IOP change over 5 years (Table 3). Per year of higher age, IOP change increased by 0.02 mmHg ($P < 0.001$). IOP change was lower in females (−0.12 mmHg; $P < 0.001$). As mean blood pressure over 5 years in the underlying cohort decreased in men but increased in women, the models for blood pressure were additionally stratified by sex. This hardly changed the effect estimates (Supplementary Table S2).

Baseline systolic blood pressure was not associated with IOP change, but a change of systolic blood pressure was positively associated with IOP change. Baseline pulse amplitude was not associated with IOP change; however, a change in pulse amplitude was. The baseline HbA1c level was not associated with IOP change, whereas the change of HbA1c level was positively associated with IOP change over 5 years.

When a stepwise backward regression analysis was performed, a correlation was observed between baseline systolic blood pressure and IOP change, in contrast to the multivariable model. The multivariable regression estimators shown previously changed little in the stepwise backward regression analysis model, and the previous shown associations remained consistent.

We analyzed the potential interaction between baseline BMI and BMI change over 5 years and did not find a statistical interaction ($P = 0.69$). Furthermore, we included baseline central corneal thickness (CCT) and change in CCT over 5 years. Between baseline and follow-up, the device for CCT measurement was changed. We first subtracted the equipment-related changes and then calculated the difference between baseline and follow-up. The results were comparable to the results obtained before. The results must nevertheless be viewed with caution due to the different measuring devices (Supplementary Table S3).

## Discussion

This study investigated IOP changes with regard to age, sex, and changes in cardiovascular parameters over 5 years. Over these 5 years, IOP in the right eye increased by 0.73 mmHg. The main results of the multivariable regression analysis demonstrated that age and sex were associated with IOP change, with females having slightly lower IOP values than male participants. BMI change and change in systolic blood pressure were positively associated with IOP change, whereas baseline BMI and change in pulse amplitude were negatively associated. There was an association between change in HbA1c level with IOP change.

IOP values in this study population are similar to those of other European studies examining IOP in a large cohort.[25] The findings of this study regarding BMI and systolic blood pressure are like those of a Chinese longitudinal study on IOP change over 4 years. As participants' blood pressure and BMI increased, IOP increased.[22] Results from the Beijing Eye

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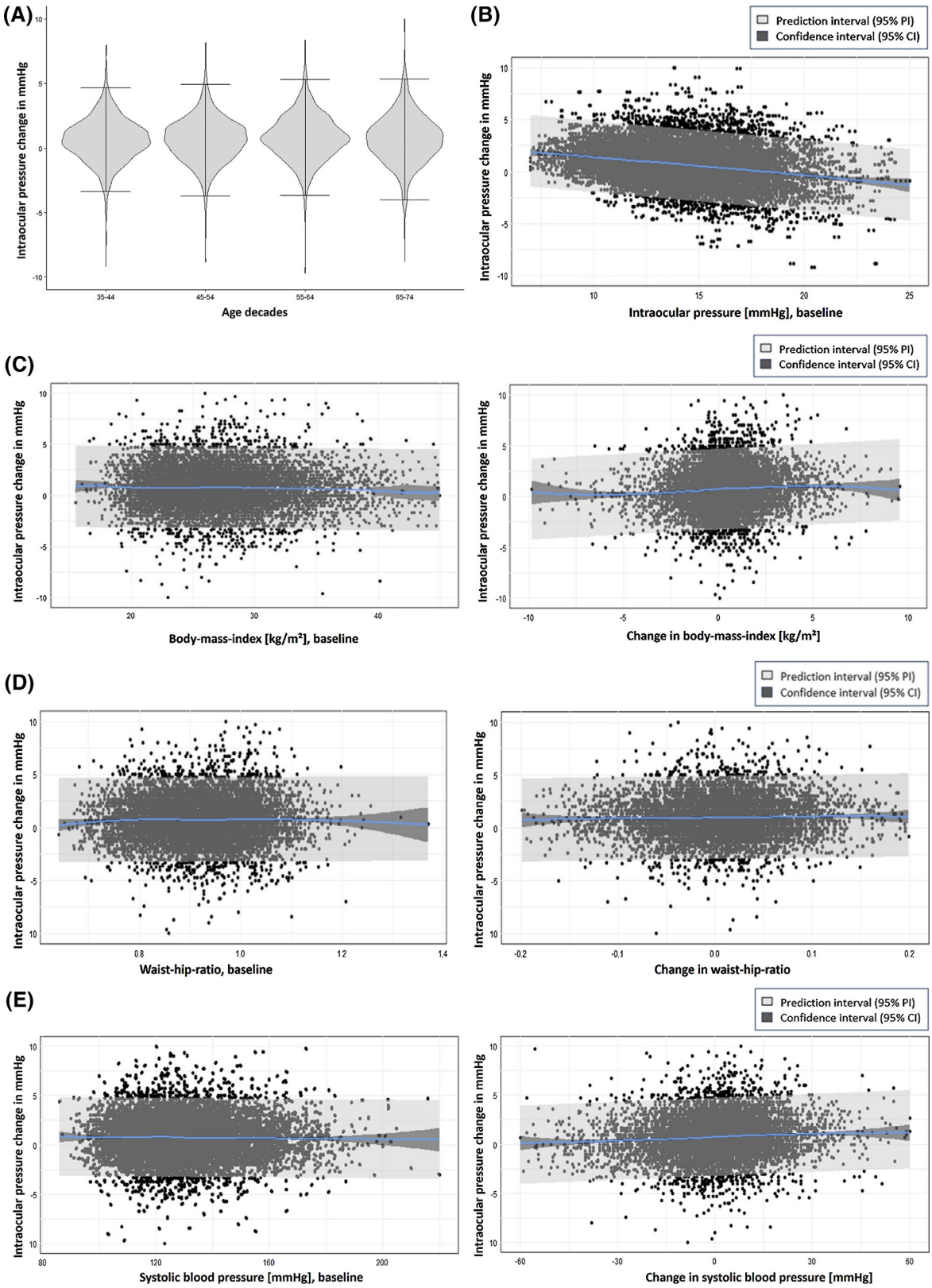


**Figure 2.** Association between IOP change over 5 years in the right eye and (**A**) age decades; (**B**) intraocular pressure (baseline); (**C**) BMI (baseline)/BMI change over 5 years; (**D**) waist-to-hip ratio (baseline)/waist-to-hip ratio change over 5 years; (**E**) systolic blood pressure (baseline)/systolic blood pressure change over 5 years; (**F**) diastolic blood pressure (baseline)/change of diastolic blood pressure; (**G**) pulse amplitude (baseline)/change of pulse amplitude; (**H**) percent of HbA1c level (baseline)/change of HbA1c level over 5 years. Results are based on the population-based Gutenberg Health Study ($N = 9590$ eyes; 2007–2017).

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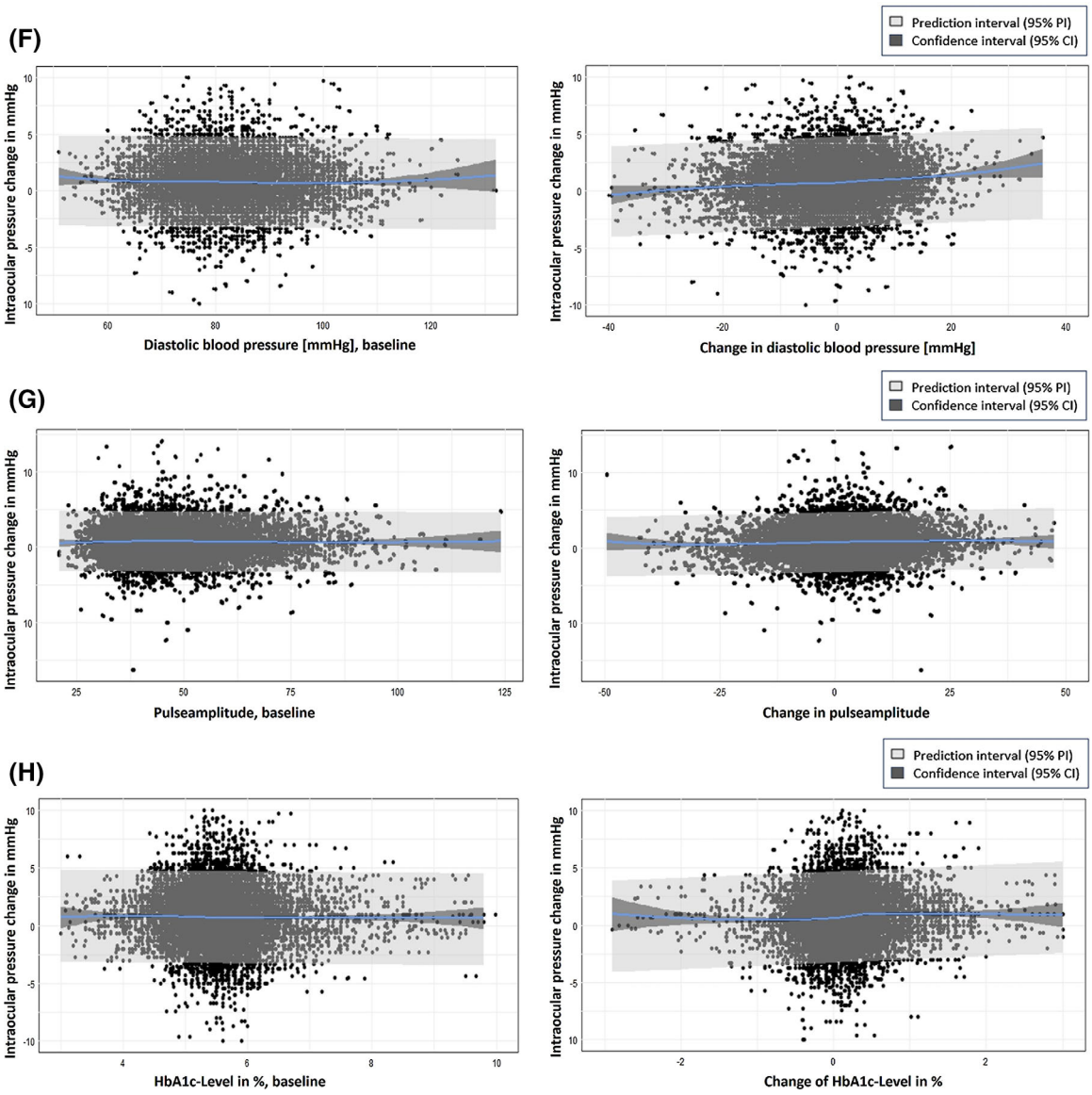


**Figure 2.** Continued.

study (2355 participants) support these findings, showing an association between change in IOP over 5 years and greater changes in mean blood pressure and BMI.[26]

The Beaver Dam Eye Study examined systemic blood pressure and IOP longitudinally over 5 years and found an association between changes in systemic blood pressure and IOP.[27] The underlying mechanism may be that higher systolic blood pressure increases aqueous humor production due to higher blood pressure in the ciliary artery.[28] Furthermore, the change in pulse amplitude was associated. This association additionally illustrates the influence of aqueous humor production on IOP, which is influenced by blood flow and pressure change within its arteries.[29]

Several cross-sectional studies have reported a similar relationship between BMI and IOP.[8,30] We showed that a change in BMI goes along with a subsequent increase in IOP. One hypothesis is that obesity increases oxidative stress, leading to degeneration of the trabecular meshwork and increased blood viscosity and episcleral venous pressure.[22] Furthermore, obesity can lead to endothelial and autonomic dysfunction. This can lead to altered blood flow to the eye and unstable perfusion.[31] Additionally, increased corticosteroid secretion in overweight individuals could potentially explain the association.[32]

Interestingly, baseline BMI was negatively associated with IOP change over 5 years. This may be explained by the fact that people with higher body weight have already experienced changes due to oxidative stress in the past with consecutive IOP elevation. Thus, the further elevation of IOP was less pronounced.

The baseline waist-to-hip ratio showed a univariable positive association with IOP change. This result is consistent with other cross-sectional studies.[8,9] This association could arise from the previous reasoning regarding the association between higher BMI and higher IOP, as a greater waist-to-hip ratio may also be a measure of overweight.

Cross-sectional studies have reported an association between diabetes and higher IOP.[16] The observed IOP

**Table 3.** Association Analysis Between Cardiovascular Risk Factors and a Change in IOP Over 5 Years

| | Univariable | | | | Multivariable | | | Stepwise Backwards Selection | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | *B* | 95% CI | *P* | Pearson's Correlation (*R*) | *B* | 95% CI | *P* | *B* | 95% CI | *P* |
| Female sex, baseline | −0.05 | −0.11 to 0.00 | 0.07 | — | −0.12 | −0.22 to −0.02 | 0.02 | −0.14 | −0.21 to −0.07 | <0.001 |
| Age, baseline | 0.01 | 0.00–0.01 | <0.001 | 0.04 | 0.02 | 0.01–0.02 | <0.001 | 0.02 | 0.01–0.02 | <0.001 |
| IOP, average, baseline and follow-up | 0.06 | 0.04–0.07 | <0.001 | 0.08 | 0.09 | 0.08–0.11 | <0.001 | 0.09 | 0.08–0.11 | <0.001 |
| BMI | | | | | | | | | | |
| Baseline | −0.02 | −0.02 to −0.01 | <0.001 | −0.03 | −0.03 | −0.04 to −0.02 | <0.001 | −0.02 | −0.03 to −0.02 | <0.001 |
| 5-year change | 0.09 | 0.08–0.11 | <0.001 | 0.08 | 0.07 | 0.05–0.09 | <0.001 | 0.07 | 0.05-0.10 | <0.001 |
| Waist-to-hip ratio | | | | | | | | | | |
| Baseline | 1.20 | 0.63–1.76 | <0.001 | 0.01 | 0.10 | −0.59 to 0.80 | 0.77 | — | — | — |
| 5-year change | 0.04 | −0.03 to 0.11 | 0.26 | 0.03 | 0.53 | −0.13 to 1.19 | 0.12 | — | — | — |
| Systolic blood pressure (per 10 mmHg) | | | | | | | | | | |
| Baseline | −0.00 | −0.03 to 0.02 | 0.82 | −0.02 | −0.00 | −0.01 to 0.00 | 0.20 | −0.00 | −0.01 to 0.00 | 0.002 |
| 5-year change | 0.13 | 0.11–0.15 | <0.001 | 0.09 | 0.02 | 0.01–0.02 | <0.001 | 0.02 | 0.01–0.02 | <0.001 |
| Pulse amplitude (per 10 mmHg) | | | | | | | | | | |
| Baseline | −0.03 | −0.01 to 0.00 | 0.07 | −0.01 | −0.00 | −0.01 to 0.00 | 0.49 | — | — | — |
| Change | 0.09 | 0.01–0.01 | <0.001 | 0.06 | −0.01 | −0.02 to −0.01 | 0.00 | −0.01 | −0.02 to −0.01 | <0.001 |
| HbA1c | | | | | | | | | | |
| Baseline | 0.01 | −0.05 to 0.08 | 0.72 | −0.02 | 0.06 | −0.01 to 0.12 | 0.10 | — | — | — |
| Change | 0.15 | 0.06–0.23 | 0.001 | 0.06 | 0.12 | 0.03–0.21 | 0.01 | 0.09 | 0.01–0.16 | 0.02 |

Data are from the German population-based Gutenberg Health Study (2007–2017; $N = 9633$ individuals). Linear regression analyses were performed using generalized estimating equation estimations. Dashed lines separating the three models. CI, confidence interval.

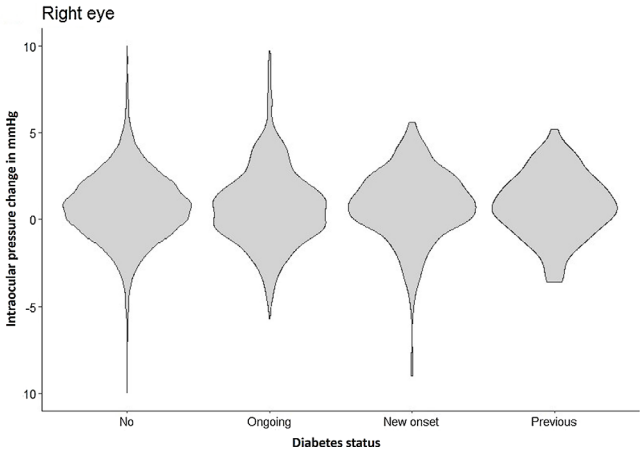


**Figure 3.** Association between IOP change in the right eye and diabetes status, based on the population-based Gutenberg Health Study ($N = 9590$; 2007–2017).

increase in cross-sectional studies might be due to elevated IOP in neovascular glaucoma, which is unlikely to occur early after the onset of diabetes. Another reason could be lower glucose control in diabetic patients, which may affect biomechanical properties of the cornea and may lead to increased IOP measures.[33] Another hypothesis suggests that autonomic dysfunction due to diabetes might increase IOP.[34,35] Evidence of an association between baseline and change in HbA1c level and IOP change was demonstrated in this study. This may be due to an increased glucose concentration in the aqueous humor. The aqueous humor flows through the trabecular meshwork and can lead to changes in its components. Evidence of an association between baseline and change in HbA1c level and IOP change was demonstrated in this study. This may be due to an increased glucose concentration in the aqueous humor. The aqueous humor flows through the trabecular meshwork and can lead to changes in its components and its biochemical properties due to the high glucose content.[36]

Higher IOP at an older age was reported to be associated with an increase in IOP in other studies investigating a similar age range.[14] We found a correlation between IOP increase and baseline age ($P < 0.001$); however, comparing IOP across various studies is difficult due to different age groups, ethnicities, and comorbidities. Older individuals tend to show more pronounced age-related ocular changes, including a decline in aqueous humor secretion and outflow facility, as well as alterations in corneal characteristics.[37,38]

Our results showed significant sex differences related to IOP and IOP change with higher values in men. Moreover, higher IOP values in men have been shown in other studies, as well[8,18]; however, some studies have shown opposite results.[17] The exact reasons for this sex difference are not well understood. A possible reason for the higher IOP values in men is that the higher testosterone levels in men may lead to higher IOP.[39] In turn, certain hormones could also lead to altered IOP in women. Fluctuations in hormone levels during the menstrual cycle in women are reported to lead to changes in IOP.[40] The larger corneal diameter in men may also lead to higher IOP measurements in men.[41]

## Strengths and Limitations

This study analyzed data from a large population-based representative sample. The Gutenberg Health Study is one of the first to investigate the change in IOP and possible cardiovascular associations longitudinally over 5 years. However, our study has some limitations that must be considered. First, the included GHS subjects were mainly of Caucasian origin; therefore, the results cannot be generalized to other ethnicities. Additionally, IOP was measured only once, and we could not consider individual intra- and interday fluctuations. The GHS was able to examine most of the study

participants at a similar time of day and the same season at baseline and 5-year examination. Although noncontact tonometry is commonly used to assess IOP in clinical settings, it is not entirely consistent with the Goldmann applanation tonometry, which is considered the reference standard. This difference may have influenced the results of this study.

## Conclusions

This study reported a positive association between IOP change over 5 years and change in BMI and systolic blood pressure. A higher baseline BMI was associated with a lower IOP increase within 5 years. This suggests that alterations in BMI and systolic blood pressure can impact IOP over an extended period and that these cardiovascular parameters should be monitored in IOP management.

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