Optic Disc Hemorrhages Detected in a Large-scale Eye Disease Screening Project

Tetsuya Yamamoto[1], MD, Aiko Iwase[1,2], MD, Kazuhide Kawase[1], MD, Akira Sawada[1], MD, and Kyoko Ishida[1], MD

1: Department of Ophthalmology, Gifu University School of Medicine

2: Department of Ophthalmology, Tajimi Municipal Hospital

Send all correspondence to: Tetsuya Yamamoto, MD,

Department of Ophthalmology,

Gifu University School of Medicine,

40 Tsukasa-machi, Gifu-shi, Japan, 500-8705

Tel: +81(Japan)-58-267-2272

Fax: +81(Japan)-58-265-9012

E-mail: mmc-gif@umin.ac.jp

Abstract

Purpose: To investigate the prevalence and characteristics of optic disc hemorrhages.

Materials and Methods: We took IMAGEnet fundus photographs of 14,779 participants, aged 40 years or older in a large-scale eye disease screening project conducted in Tajimi, Japan. A single researcher reviewed all of the photographs for the presence of ocular abnormality in the optic nerve head and retina, paying special attention to the presence or absence of optic disc hemorrhages. Glaucomatous optic neuropathy was diagnosed based on the presence of nerve fiber layer defects and/or the appearance of the optic disc.

Results: Fundus photographs of 13,965 cases (27,930 eyes) were successfully reviewed bilaterally. We found disc hemorrhages at 92 locations of 92 (0.3%) eyes of 88 (0.6%) cases. Twenty-four hemorrhages of 23 (26%) cases were found in bilateral non-glaucoma cases and the remaining 68 hemorrhages of 65 (74%) cases were found in glaucoma cases. The prevalence of disc hemorrhages was 8.2% in 793 glaucoma cases and 0.2% in non-glaucoma cases. Hemorrhages developed significantly more frequently in females and in the elderly. The hemorrhages were predominantly found in the inferotemporal and superotemporal regions. The intraocular pressure was less than 20 mmHg in all cases. The mean intraocular pressure was 15.0 mmHg for glaucoma cases with hemorrhages and 13.9 mmHg for non-glaucoma cases with hemorrhages.

Conclusion: Disc hemorrhages occur more frequently in females, in elderly persons, and in glaucoma cases in Japanese aged 40 or older. The intraocular pressure of the eyes with disc hemorrhages is close to that of the normal population.

Key Words: Optic disc hemorrhage, Glaucoma, Epidemiology, Tajimi Study

Introduction

A small, often splinter-shaped hemorrhage may be present on the optic disc in some eyes, especially those with open-angle glaucoma.[1-9] The characteristics of a disc hemorrhage in a series of clinical cases or in subjects of several population-based surveys have been reported.[3,10,11] They include: tendency to develop in the temporal inferior quadrant,[2] in glaucoma eyes with a relatively low intraocular pressure,[2,6,9] especially in the area adjacent to a rim notching, and in females at age 60 years or older.[12]

Several investigators[13-16] have emphasized the pathogenic role of disc hemorrhages in glaucomatous optic neuropathy, while some researchers[17,18] believe that disc hemorrhage is unrelated to glaucoma progression. Drance et al.[13] pointed out that visual field defects are more likely to progress in eyes with a disc hemorrhage in chronic simple glaucoma. Bengtsson et al.[3] proposed that hemorrhages occur in all cases of progressive glaucomatous optic neuropathy. Our group[16] found that disc hemorrhage is a significant risk factor for the progression of glaucoma using a Kaplan-Meier life-table analysis.

Since normal-tension glaucoma is known to be the most prevalent subtype of glaucoma among Japanese[19,20], it would be valuable to compare the characteristics of disc hemorrhages, such as the prevalence in the general population and in glaucoma patients, and the distribution of the intraocular pressure, between Japanese and other ethnicities. The present study focused on the prevalence and characteristics of disc hemorrhages in Japanese.

Materials and Methods

The data used in the present study were obtained at the Eye Health Care Project in Tajimi and were provided by the Japan Glaucoma Society, which conducted a large-scale eye disease screening project. Our usage of the data was approved by the Japan Glaucoma Society, which has contracted with Tajimi City so that the society can use the data strictly for scientific purposes as long as subject anonymity is preserved. Additionally, informed consent was obtained from all participants before participating in the eye disease screening project and all of them gave the Japan Glaucoma Society permission to use the individual data for scientific research on condition of anonymity. The details of the Eye Health Care Project in Tajimi will be published elsewhere.[19] In short, the Eye Health Care

Project in Tajimi was a large-scale eye disease screening project conducted in Tajimi City, Gifu, Japan between September 2000 and October 2001. The Eye Health Care Project was comprised of two study populations: one consisted of 4,000 randomly selected citizens aged 40 or older who underwent a detailed ophthalmological check-up, and the other consisted of a general screening for the general population aged 40 or older. The 4,000 selected citizens were not subjected in the present study. In the latter, the following ophthalmological examinations were conducted for both eyes: visual acuity testing, refractometry with a refractometer (KP-8100PA, Topcon, Tokyo, Japan), corneal thickness measurement with an SP-2000P (Topcon, Tokyo, Japan), perimetry with an FDT screener (Humphrey Instruments, San Leandro, CA) with the C-20-1 screening program, 45-degree fundus photography with an IMAGEnet 6S (Topcon, Tokyo, Japan), applanation tonometry with a Goldmann tonometer, slit-lamp biomicroscopy, and a van Herick test. In addition, the participants were requested to fill out a questionnaire including their medical history, and their systemic blood pressure, body weight, and height were also measured. While the subject's ethnicity was not determined in the questionnaire, practically speaking, all of the participants were ethnic Japanese. The general screening targeted 50,165 citizens aged 40 or older. Of the 50,165 citizens, 14,779 participated in the screening, giving a response rate of 29.5%.

In the present study, all of the 45-degree IMAGEnet fundus photographs were reviewed for the presence of ocular abnormality in the optic nerve head and the retina of the posterior pole by one of the authors (TY), who was also one of the chief investigators for the Eye Health Care Project in Tajimi. The reviewer paid special attention to the presence or absence of optic disc hemorrhages and recorded the clock position if they existed. The subject information, except for the bilateral fundus photographs, was masked to the reviewer. We defined optic disc hemorrhages as a hemorrhage or hemorrhages of any shape involving an optic disc in eyes without any additional retinal hemorrhages in the retina. Glaucomatous optic neuropathy was diagnosed based on the presence of nerve fiber layer defects and/or the following disc features: the vertical cup/disc ratio of optic nerve head more than or equal to 0.7, the rim width at superior portion (11- 1 hour) or inferior portion (5 - 7 hour) less than or equal to 0.1 of disc diameter, and a 0.2-difference in the cup/disc ratio between both eyes. Each optic disc was classified into one of the following three categories based solely on the disc and nerve fiber layer appearance: glaucomatous optic neuropathy, non-glaucomatous abnormality, and

normal. In this, glaucoma implies a case with glaucomatous optic neuropathy.

Results

Of the 14,779 participants of the Tajimi Eye Disease Screening, 45-degree IMAGEnet fundus photographs of 28,396 eyes of 14,431 cases were successfully reviewed. A total of 1,162 eyes of 814 cases were not used because the fundus photos were unavailable for 312 eyes and because the photos were of poor quality for 850 eyes. In the present study, we only included cases in whom the fundus photos were successfully reviewed bilaterally. Thus, the study population of this study included 27,930 eyes of 13,965 cases. The age and sex distribution of the study population is shown in Table 1. Of the 13,965 cases, we found disc hemorrhages at 92 locations of 92 (0.3%) eyes of 88 (0.6%) cases. Four (4.5%) cases were bilateral and 84 (95.5%) cases were unilateral. Fifty-one (55%) hemorrhages developed in the right eye and 41 (45%) in the left.

Of the total of 13,965 cases in the current study population, we found 793 (5.7%) glaucoma cases: 476 (3.4%) bilateral cases and 317 (2.3%) unilateral cases. Of 92 disc hemorrhages, 24 hemorrhages of 23 (26%) cases developed in bilateral non-glaucoma cases and the remaining 68 hemorrhages of 65 (73%) cases developed in glaucoma cases. Of the 65 glaucoma cases, 61 were undiagnosed cases, 3 treated glaucoma cases and one had a previous history of glaucoma. In the glaucoma cases, 60 hemorrhages developed in eyes with glaucomatous optic neuropathy and 8 in eyes without a sign of glaucomatous optic neuropathy. The age and sex distribution of disc hemorrhages found is shown in Table 2. A hemorrhage developed significantly more frequently in females ($p=0.0141$, chi-square test) and in the elderly ($p=0.0002$, chi-square test). The prevalence of disc hemorrhages was 8.2% in glaucoma cases and 0.2% in non-glaucoma cases (Table 2).

The clock positions of disc hemorrhages after the left eyes were converted to the right as a mirror image are shown in Figs. 1-3. Figure 1 presents the glaucoma cases, Fig. 2 presents the non-glaucoma cases, and Fig. 3 presents all of the cases. The hemorrhages were predominantly found in the inferotemporal and superotemporal regions. When the sites of disc hemorrhages were compared between the glaucoma cases and the non-glaucoma cases, the rate of developing the hemorrhage at the inferotemporal and superotemporal regions, *i.e.*, at the 7, 8, 10, and 11 o'clock positions of the right eye, or at the 1, 2, 4, and 5 o'clock of the left, was significantly higher in cases of

glaucoma ($p<0.0001$, Fisher's direct probability test).

The distribution of the intraocular pressure of the eyes with a disc hemorrhage is shown in Fig. 4. The intraocular pressure was less than 20 mmHg in all cases. The mean (± standard deviation) intraocular pressure was 15.0 ± 2.1 mmHg for glaucoma cases with hemorrhages including three treated cases, in which the intraocular pressure was 14, 16, and 16 mmHg, respectively. The mean intraocular pressure was 13.9 ± 2.3 mmHg and 14.7 ± 2.2 mmHg for non-glaucoma cases with hemorrhages and all cases with them, respectively.

As for the medical history of the participants, 18 cases reported a positive history of systemic hypertension: 14 with current medical therapy and 4 without; and 3 of the glaucoma cases had had diabetes mellitus that had been treated previously. In the non-glaucoma cases, 7 cases reported a positive history of systemic hypertension: all on medical treatment; and 2 had had previous treatment for diabetes mellitus. The systemic, systolic blood pressure, excepting cases with treatment of systemic hypertension, was 132.1 ± 22.1 mmHg and 133.5 ± 21.2 mmHg for glaucoma cases and non-glaucoma, respectively. The diastolic pressure was 78.1 ± 10.8 mmHg and 77.8 ± 10.1 mmHg, respectively.

Discussion

The present study revealed that the prevalence of disc hemorrhages was 0.6% in Japanese aged 40 or older: 8.2% for glaucoma cases and 0.2% for non-glaucoma cases. We cannot detect a disc hemorrhage without looking at the optic disc, which may cause bias in diagnosing glaucomatous optic neuropathy. However, we found a 5.7% prevalence of glaucomatous optic neuropathy in the present study, which is close to a 6.0% prevalence of open-angle glaucoma in the Tajimi Study[19]. The 0.6% overall prevalence rate is identical to that reported in a health consultation center-based study (35/5,967 cases) by Sugiyama et al. [12], although the age distribution of the two studies was different. The 0.6% rate is similar to or lower than that reported in several population-based surveys[3,10,11] performed in the West. The Dalby Study[3] found 12 (0.8%) cases with disc hemorrhages in a study of 1,511 participants. The Beaver Dam Eye Study[10] found disc hemorrhages in 46 (0.9%) cases of 4,926 participants. The Blue Mountains Eye Study[11] found disc hemorrhages in 55 (1.4%) cases of 3,654 participants. In contrast to the similar prevalence rate found among different

populations, the predominance of disc hemorrhages in glaucoma cases in the present study is significant: 74% of the present cases with disc hemorrhages had glaucomatous optic neuropathy. The Beaver Dam Eye Study[10] reported that only 2 (4.3%) of cases with disc hemorrhages showed definite glaucoma, which was defined as a combination of at least two of the following criteria: abnormal visual field, large or asymmetric cup-to-disc ratio, high intraocular pressure and or singly a history of glaucoma with treatment. The ratio of open-angle glaucoma in cases with disc hemorrhages was 30% in the Blue Mountains Eye Study, where open-angle glaucoma was basically defined as typical visual field defects on the Humphrey Central 30-2 test and enlarged cupping equal to or greater than 0.7, or cup-to-disc asymmetry between the two eyes.[11] The Dalby Study[3] found 7 (58%) glaucoma cases with disc hemorrhages and 5 non-glaucoma cases with them, but the number of cases with disc hemorrhages was relatively small. Although the definition of glaucoma is different, the discrepancy between the Western population-based studies and ours suggests that Japanese glaucoma patients are more likely to develop a disc hemorrhage than are Caucasian or African-American patients. The epidemiological finding that the most prevalent subtype of glaucoma in the Japanese population is normal-tension glaucoma,[19,20] which is known to be frequently associated with disc hemorrhages,[6,9] supports the large percentage of disc hemorrhages occurring in glaucoma cases in the present study.

The mean intraocular pressure of the glaucoma eyes with disc hemorrhages was 15.0 mmHg and the maximum was 19 mmHg in the present study. These values were close to those of the normal population. Thus, it is very likely that most of glaucoma patients with disc hemorrhages suffer from normal-tension glaucoma although the full complement of diagnostic procedures including a 24-hour measurement of the intraocular pressure and brain imaging were not performed. The mean intraocular pressure of the cases with and without disc hemorrhages was reported to be 17.7 mmHg and 16.7 mmHg, respectively, in glaucoma cases in the Blue Mountains Eye Study.[11] A mean of 19.8 mmHg, ranging from 13 to 30 mmHg, was also found in untreated glaucoma cases in the Dalby Study[3] (present authors' calculation based on a histogram shown in the cited paper). The Beaver Dam Eye Study[10] did not mention the intraocular pressure level of cases with disc hemorrhages. Therefore, the intraocular pressure of eyes with a disc hemorrhage seems to be lower in the present study than that reported in other population-based studies.

Hemorrhages were found most often in the temporal side, especially in the inferotemporal

region, followed by the superotemporal region. This is similar to findings in several previous studies.[2,3,12] In glaucoma cases, disc hemorrhages occurred more frequently in the inferotemporal and superotemporal regions. This is also consistent with previous studies.[2,11] These regions are known to be the sites where the earliest glaucomatous changes are evident. The predominant development of disc hemorrhages in the site where the glaucoma change occurs suggests a correlation between disc hemorrhages and glaucomatous optic neuropathy.

We also found that disc hemorrhages were most prevalent in females, which is consistent with studies by Bengtsson et al, [3] Sugiyama et al, [12] and the Beaver Dam Eye Study.[10] However, normal-tension glaucoma is not reported to be more prevalent in Japanese females. To better understand the pathogenic role of disc hemorrhages in glaucomatous optic neuropathy, this gender discrepancy in disc hemorrhage and the similarity in the prevalence of normal-tension glaucoma between the sexes should be further studied.

It should be noted that the present study employed a subjective diagnosis of glaucomatous optic neuropathy by a single expert, and that there was a low response rate among the participants. As for the diagnostic procedure, the glaucoma specialist was also a member of the disc reading committee of the Tajimi Study, which reported a similar level of glaucoma prevalence, as determined by a consensus among six experts and by objective diagnostic criteria. [19] In the present study, an expert read all IMAGEnet photographs of a total of 27,930 eyes of 13,965 cases during a 6-week period. Thus, a high level of consistency would be expected. However, the low response rate implies a bias because of less participation of those who had previously had ophthalmic care and relatively higher participation rate of citizens with a family history of glaucoma. The participation of a great number of citizens may overcome this flaw in future studies. In fact, it is well known that the majority of normal-tension glaucoma cases found in population-based studies show no history of glaucoma care and little awareness of the disease. [20]

In conclusion, we confirmed that disc hemorrhages occur frequently in females, in elderly persons, and in glaucoma cases in Japanese aged 40 or older. The intraocular pressure of the eyes with disc hemorrhages was close to that of the normal population. Disc hemorrhages occur more frequently at the inferotemporal and superotemporal regions in glaucoma cases than in non-glaucoma cases. The pathogenic role of disc hemorrhage in glaucomatous optic neuropathy warrants further

investigation.

Acknowledgement

The authors wish to express their deep gratitude to Ms. Megumi Onda for her devoted secretarial assistance.

References

1. Susanna R, Drance SM, Douglas GR. Disc hemorrhage in patients with elevated intraocular pressure. Occurrence with and without field changes. *Arch Ophthalmol*. 1979;97:248-285.

2. Airaksinen PJ, Mustonen E, Alanko HI. Optic disc hemorrhages. Analysis of stereophotographs and clinical data of 112 patients. *Arch Ophthalmol*. 1981;99:1795-1801.

3. Bengtsson B, Holmin C, Krakau CET. Disc haemorrhage and glaucoma. *Acta Ophthalmol. (Copenh)* 1981;59:1-14.

4. Gloster J. Incidence of optic disc hemorrhages in chronic simple glaucoma and ocular hypertension. *Br J Ophthalmol*. 1981;65:452-456.

5. Shihab ZM, Lee P, Hay P. The significance of disc hemorrhage in open-angle glaucoma. *Ophthalmology* 1982;89:211-213.

6. Kitazawa Y, Shirato S, Yamamoto T. Optic disc hemorrhage in low-tension glaucoma. *Ophthalmology* 1986;93:853-857.

7. Diehl DLC, Quigley HA, Miller NR, et al. Prevalence and significance of disc hemorrhage in a longitudinal study of glaucoma *Arch Ophthalmol*. 1990;108:545-550.

8. Hendrickx KH, van den Enden A, Rasker MT, et al. Cumulative incidence of patients with disc hemorrhages in glaucoma and effect of therapy. *Ophthalmology* 1994;101:1165-1172.

9. Drance SM. Disc hemorrhages in the glaucomas. Surv Ophthalmol. 1989;33:331-337.

10. Klein BEK, Klein R, Sponsel WE, et al. Prevalence of glaucoma. The Beaver Dam Eye Study. *Ophthalmology* 1992;99:1499-1504.

11. Healey PR, Mitchell P, Smith W, et al. Optic disc hemorrhage in a population with and without signs of glaucoma. *Ophthalmology* 1998;105:216-223.

12. Sugiyama K, Tomita G, Kawase K, et al. Disc hemorrhage and peripapillary atrophy in apparently healthy subjects. *Acta Ophthalmol Scand*. 1999;77:139-142.

13. Drance SM, Fairclough M, Butler DM, et al. The importance of disc hemorrhage in the prognosis of chronic open angle glaucoma. *Arch Ophthalmol*. 1977;95:226-228.

14. Bengtsson B. Optic disc haemorrhage preceding manifest glaucoma. *Acta Ophthalmol. (Copenh)* 1990;68:450-454.

15. Siegner SW, Netland PA. Optic disc hemorrhages and progression of glaucoma. *Ophthalmology* 1996;103:1014-1024.

16. Ishida K, Yamamoto T, Sugiyama K, et al. Disk hemorrhage is a significantly negative, prognostic factor in normal-tension glaucoma. *Am J Ophthalmol*. 2000;129:707-714.

17. Hoyng PFJ, de Jong N, Oosting H, et al. Platelet aggregation, disc hemorrhage and progressive loss of visual fields in glaucoma. *Int Ophthalmol*. 1992;16:65-73.

18. Heijl A. Frequent disc photography and computerized perimetry in open-angle glaucoma treated with pilocarpine or timolol. *Acta Ophthalmol. (Copenh)* 1991;69:217-224.

19. Iwase A, Suzuki Y, Araie M, et al. The prevalence and intraocular pressure of primary open-angle glaucoma in Japanese. The Tajimi Study. *Ophthalmology in press*

20. Shiose Y, Kitazawa Y, Tsukahara S, et al. Epidemiology of glaucoma in Japan. A nationwide glaucoma survey. *Jpn J Ophthalmol*. 1991;35:133-155.

Figure legends

Fig. 1. The clock positions of disc hemorrhages found in glaucoma cases. Sixty-eight hemorrhages were found in 68 eyes of 65 cases. No hemorrhages were found in the cup flour. S: superior, T: temporal, I: inferior, and N: nasal.

Fig. 2. The clock positions of disc hemorrhages found in non-glaucoma cases. Twenty-four hemorrhages were found in 24 eyes of 23 cases. No hemorrhages were found in the cup flour. S: superior, T: temporal, I: inferior, and N: nasal.

Fig. 3. The clock positions of disc hemorrhages found in all cases. Ninety-two hemorrhages were found in 92 eyes of 88 cases. No hemorrhages were found in the cup flour. S: superior, T: temporal, I: inferior, and N: nasal.

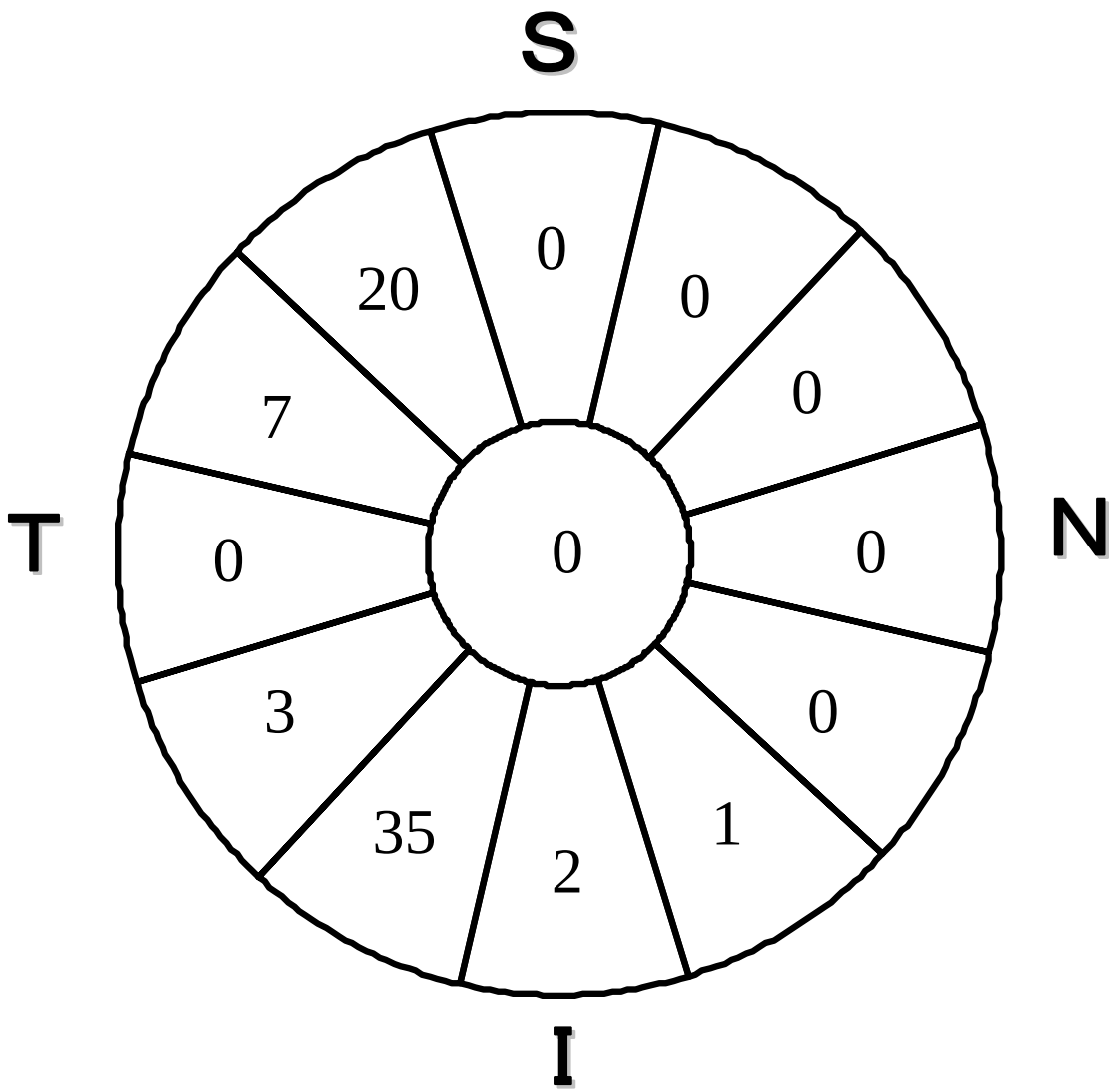
Fig. 4. The distribution of the intraocular pressure (IOP) of eyes with a disc hemorrhage. Black: glaucoma cases, gray: non-glaucoma cases, white: all cases. The mean (± standard deviation) IOP was 15.0 ± 2.1 mmHg, 13.9 ± 2.3 mmHg, and 14.7 ± 2.2 mmHg, respectively. Glaucoma cases include three treated cases, in which the intraocular pressure was 14, 16, and 16 mmHg, respectively.

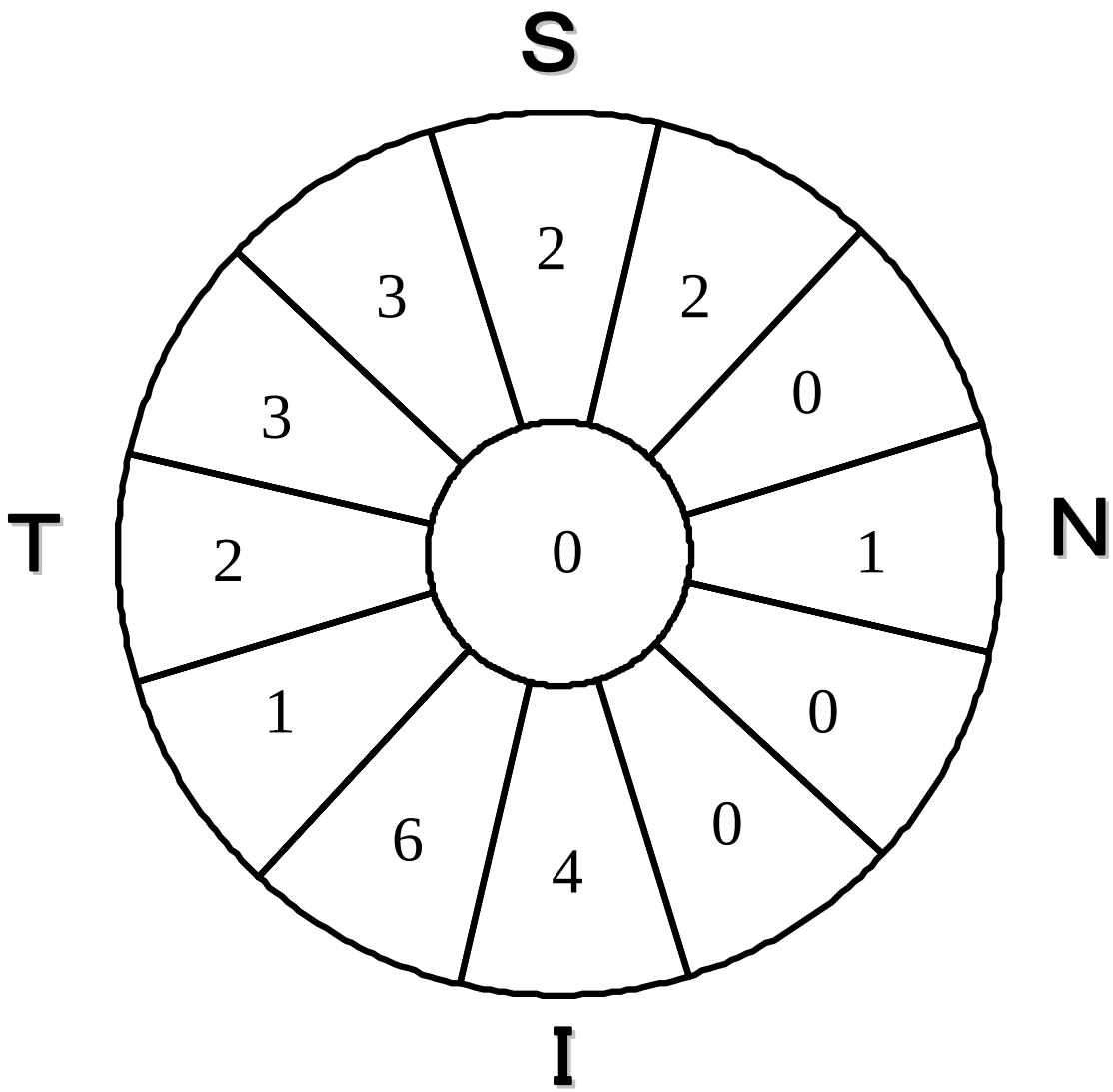
Table 1. The age and sex distribution of the study population. Upper: population targeted, middle: population screened, lower: population subjected in the present study.

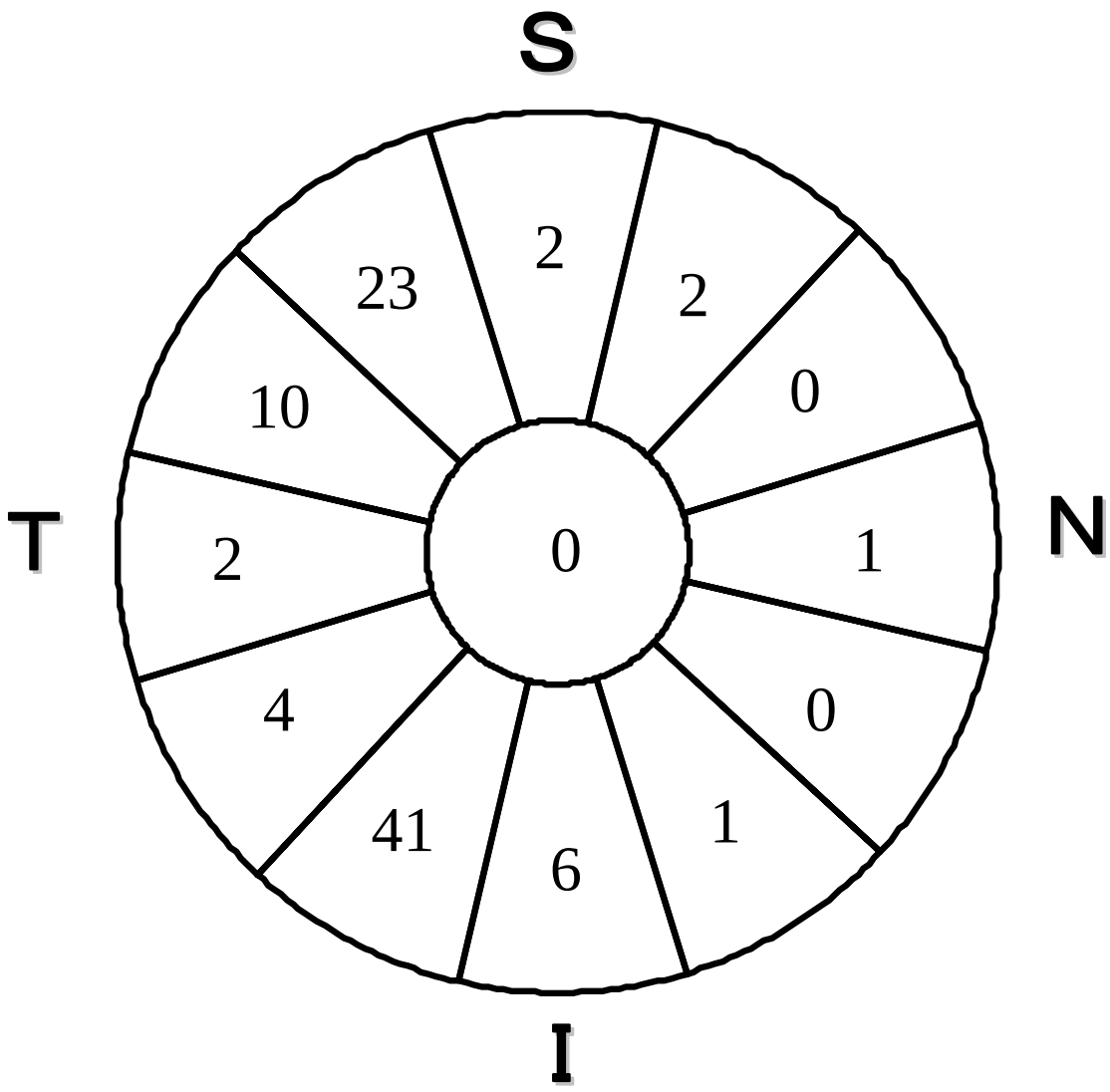
age (yrs.)	male	female	total
40-49	7,024	7,143	14,167
	996	2,024	3,020
975	1,996	2,971	
50-59	7,931	7,880	15,811
	1,531	3,131	4,662
1,479	3,056	4,535	
60-69	5,287	5,279	10,566
	1,895	2,486	4,381
1,790	2,361	4,151	
70-	3,822	5,799	9,621
	1,162	1,554	2,716
1,012	1,296	2,308	
total	24,064	26,101	50,165
	5,584	9,195	14,779
	5,256	8,709	13,965

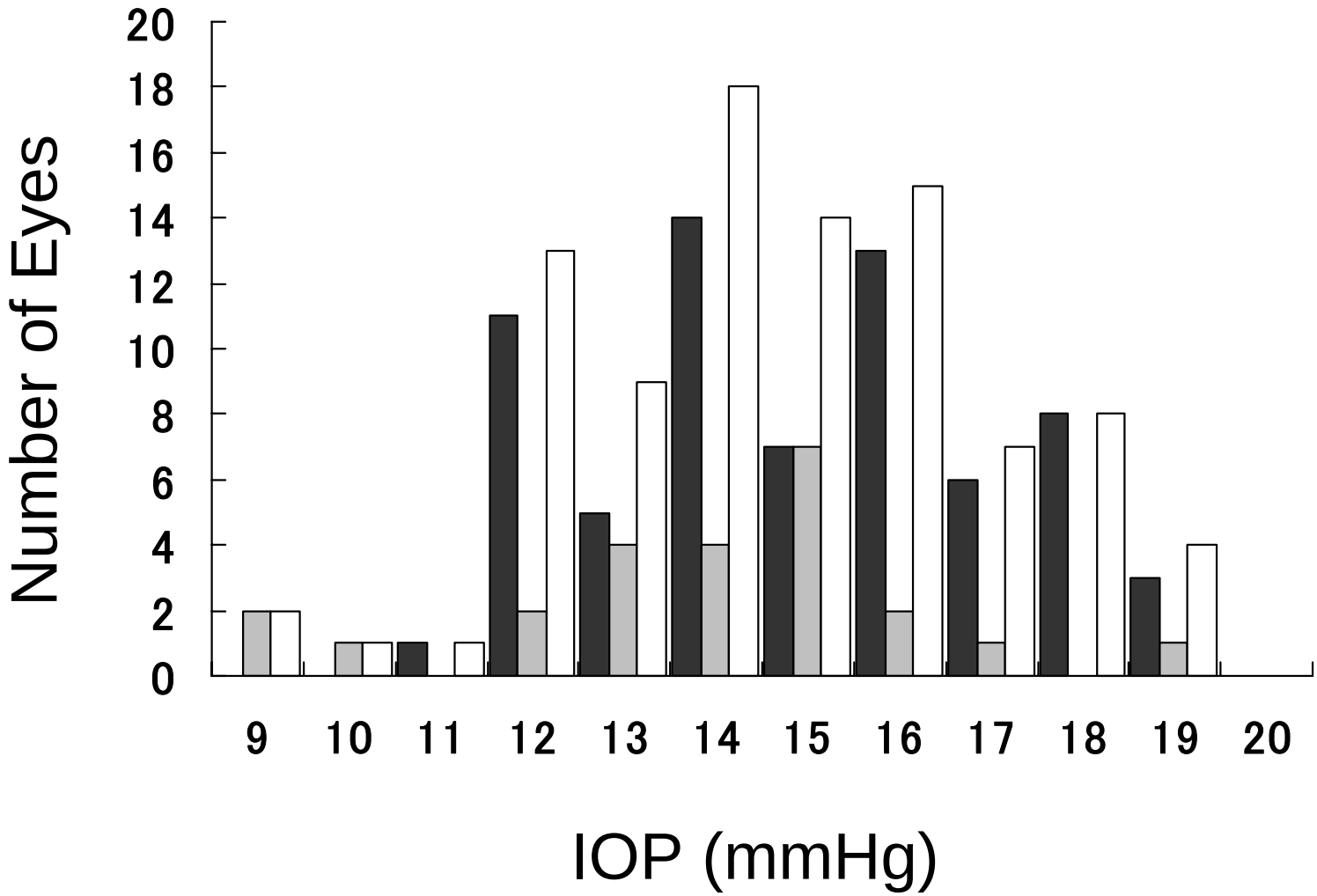
Table 2. The age and sex distribution of cases in whom disc hemorrhages were found. Upper: glaucoma cases, middle: non-glaucoma cases, lower: total cases. Number of patients with a disc hemorrhage/ number of patients studied (prevalence in percent).

age (yrs.)	male		female		total	
40-49	0/27	(0)	5/60	(8.3)	5/87	(5.7)
	0/948	(0)	2/1,936	(0.1)	2/2,884	(0.1)
	0/975	(0)	7/1,996	(0.4)	7/2,971	(0.2)
50-59	2/78	(2.6)	13/110	(11.8)	15/188	(8.0)
	0/1,401	(0)	6/2,946	(0.2)	6/4,347	(0.1)
	2/1,479	(0.1)	19/3,056	(0.6)	21/4,535	(0.5)
60-69	11/162	(6.8)	16/134	(11.9)	27/296	(9.1)
	3/1,628	(0.2)	5/2,227	(0.2)	8/3,855	(0.2)
	14/1,790	(0.8)	21/2,361	(0.9)	35/4,151	(0.8)
70-	4/90	(4.4)	14/132	(10.6)	18/222	(8.1)
	2/922	(0.2)	5/1,164	(0.4)	7/2,086	(0.3)
	6/1,012	(0.6)	19/1,296	(1.5)	25/2,308	(1.1)
total	17/357	(4.8)	48/436	(11.0)	65/793	(8.2)
	5/4,899	(0.1)	18/8,273	(0.2)	23/13,172	(0.2)
	22/5,256	(0.4)	66/8,709	(0.8)	88/13,965	(0.6)


S
0
0
0
N
0
0
1
2
35
3
0
7
20
T
I


S
2
2
0
N
1
0
0
4
6
1
T
2
3
3


S
2
2
0
1
0
1
6
41
4
2
10
23
T
N
I


Number of Eyes
0
2
4
6
8
10
12
14
16
18
20
9
10
11
12
13
14
15
16
17
18
19
20
IOP (mmHg)