

The distribution and abundance of multiple chalazia in pediatrics receiving surgery in Zhejiang province, China: a hospital-based cross-sectional study.

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Research article

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Abstract

Background: To investigate the distribution and abundance of multiple chalazia in pediatric patients that need surgical treatments.

Methods: Patients with multiple chalazia treated in a tertiary Children's Hospital were reviewed between June and December 2016. Demographic data, locations and numbers of chalazia were recorded. Data were analyzed using generalized linear models of the counts and the occurrences of chalazia. Hypotheses were tested using likelihood ratio tests appropriate for each type of data.

Results: The study included 128 subjects, most of which were 1-3 years of age. The majority of patients had bilateral chalazia (95.3%), and the proportions of patients with internal, external and marginal chalazion differed significantly (99.2%, 61.7% and 2.3% respectively). The total number of internal chalazia had a negative binomial distribution, whereas the total number of external chalazia followed a Poisson distribution. The number of internal and external chalazia did not differ significantly with gender, age, or residence of patients. Internal chalazia were located more frequently on the upper lids ($P < 0.01$). External chalazia showed no preference of localization. The average abundance of internal chalazia on each eyelid did not relate to the presence of external chalazia.

Conclusions: In Zhejiang province, China, multiple chalazia that require surgery are more common among younger children (aged 1-3 years) than older ones. The anatomical distribution varies depending on the chalazion's types. Multiple chalazia often occur bilaterally and internally. Doctors should pay more attention to the anatomical distribution to achieve a higher success rate in chalazion surgery.

Background

Children often develop chalazia, which are slowly developing lipogranulomatous lumps in the eyelids caused by obstruction of a sebaceous gland [1, 2]. An individual child may contain several lumps. In Bagheri A's study 11.8% of patients (aged 7-71 years) presented multiple chalazia [3]. Although the precise incidence rate of multiple chalazia in children is unknown, pediatric ophthalmologists have encountered this multiple presentation more and more frequently in clinical settings [4], and this disease entity is quite common in China [5].

Multiple chalazia are usually classified into 3 types according to the location of lesions – internal, external, and marginal chalazion. An internal chalazion is caused by inflammation of a tarsal meibomian gland that spreads into the conjunctiva. An external chalazion is caused by a plugged sebaceous gland that extends anteriorly to the surface of the palpebral skin and presents as a reddish subcutaneous nodule [6, 7]. A marginal chalazion arises from an inflamed gland at the eyelid margin.

Assessing the anatomical distribution of different types of multiple chalazia is essential for several reasons. First, different locations cause distinct complications or sequelae. For example, an internal chalazion can result in a hollowing of the tarsal plate, a loss of meibomian gland [8], an extratarsal

migration [9], or an astigmatism [10, 11]. An external chalazion tends to leave cosmetic damage with scarring on the eyelid, whereas a marginal chalazion may cause eyelid margin notching, trichiasis, or alopecia of the eyelashes [12]. Second, the location of a chalazion can determine the timing or method of invasive treatment. An external or marginal chalazion that presents disfiguration risks, or a large central internal chalazion that harms the vision may be considered for an earlier referral for surgical management [13]. Third, in children presenting an external chalazion, internal nodules are occasionally undetected not only by the parents but also by the health care professionals. Although an incision and curettage (I&C) operation is quite straightforward, missing nodules or incomplete drainage can cause dissatisfaction of patients, especially with children because of potential need for repeated systemic anesthesia. Knowing the spatial distribution of multiple chalazia allows strategies to be developed for estimating and treating this disease much better.

Due to the functional and aesthetic defects associated with multiple chalazia, more information is needed on the incidence and anatomical distribution of chalazia in the pediatric population. The published literatures relevant to the location of chalazia are either old or limited. In Herman's study (published in 1951) of 1693 patients ranging in ages from children to elderly, chalazia were more common on the lower lids, especially for the right eye [14]. Mustafa's study, which included 26 pediatric patients aged 3 to 16 years old, reported that chalazia were more common on the upper lid, but half of the subjects had only 2 multiple chalazia [15]. Ben reported a high occurrence of chalazion on the right upper lid (RUL) in adult patients receiving triamcinolone injection, but whether the chalazion was single or multiple was not mentioned [16]. In Knezevic's study, which recruited patients intending for botulinum toxin injection treatment, the right lower lid (RLL) was common; however, cases with infected nodules or small lesions less than 2 mm were excluded [17]. Wu's result showed a greater frequency of chalazia on the left upper lid (LUL), but didn't include patients with multiple chalazia on a single lid [18]. Collectively, these results indicate that the spatial localization and abundance of different types of multiple chalazia in children requires additional investigation.

The aim of our paper was to investigate the distribution and occurrence of multiple chalazia in pediatric patients that need surgery for their condition in Zhejiang province, China.

Methods

Study population

The patients we studied were from Children's Hospital, Zhejiang University School of Medicine, which is a regional children's clinical medical center in southeastern China that serves as the tertiary referral institution for pediatric multiple chalazia in Zhejiang province. Children that were diagnosed with multiple chalazia and examined in the Department of Ophthalmology between 1 June 2016 and 31 December 2016 were retrospectively reviewed in our study. These children were assumed to be a representative sample of all children with multiple chalazia in Zhejiang province. Our research was approved by the

Institutional Ethics Committee of Children's Hospital, and it adhered to the tenets of the Declaration of Helsinki.

Ocular evaluation

Careful ocular examination is essential for diagnosis. An internal chalazion is a firm and purplish palpable nodule on the conjunctiva when the eyelid is everted. Sometimes a chronic internal chalazion develops into a pedicled granuloma that exceeds the palpebral fissure. An external chalazion is obvious on the eyelid skin and appears as a red, elastic nodule with well-defined borders. A marginal chalazion is a small bump along the lid margin. A chalazion is usually non-tender and non-fluctuant, but if infected, a chalazion is painful and red.

Clinical managements and data collection

Patients were recommended to have warm compresses on lids 4 times a day. If local infection was considered, topical treatment with levofloxacin eye drops 5 mg/mL (Cravit; Santen, Japan) 4 times a day and/or oral azithromycin 10 mg/kg (Zithromax; Pfizer, USA) once a day for 3 days would be given. For lesions unresponsive to conservative treatments, lasting for more than 2 months, or showing potential visual or cosmetic risks, I&C surgeries under systemic anesthesia were performed. The specimens were submitted for histopathology examinations to confirm the diagnosis.

To count lesions accurately, we included only patients that had chalazion surgeries because the calculation can then be done under anesthesia. We collected the following information for analysis: age, gender, residence, type of chalazion, number and location of lesions, duration of disease/onset time defined by the guardians, and past history.

Exclusion criteria

We excluded patients whose chalazion received palliative incision or was spontaneously broken right before I&C, and those with skin findings on the eyelid caused by idiopathic facial aseptic granuloma (IFAG), acne, seborrhea, rosacea or atopy.

Statistical Analysis

Statistical analyses were performed using R software version 4.0.2 (Vienna, Austria. <https://www.R-project.org/>.) We analyzed the counts of chalazia using two classes of statistical models, one for the total number of chalazia observed at all eyelid locations and another for the number of chalazia observed at each eyelid location. The latter observations are needed to estimate the anatomical distribution of chalazia. The counts of internal and external chalazia were analyzed separately.

To be more specific, we assumed that the total number N of chalazia at all eyelid locations had either a Poisson distribution or a negative binomial distribution, whose mean μ was allowed to differ among patients of different gender, age category, or residence. That is, we assumed either

$$N \sim \text{Poisson}(\mu)$$

where $\log(\mu) = \beta^T X$ specifies the mean as a function of observed covariates X and their effects β , or

$$N \sim \text{Negative Binomial}(\mu, \alpha)$$

where α is a positive, scalar-valued parameter that indicates the level of extra-Poisson variation in N . Our choice of Poisson or negative binomial models was based on an assessment of goodness of fit.

To estimate and make inferences about the anatomical distribution of chalazia, we conditioned on N and assumed the following model:

$$Y_1, Y_2, Y_3, Y_4 \sim \text{Multinomial}(p_1, p_2, p_3, p_4)$$

where Y_1, Y_2, Y_3 and Y_4 denote the numbers of chalazia observed at each of four eyelid locations (RUL, RLL, LUL, and LLL, respectively) and where p_1, p_2, p_3 and p_4 denote parameters for the proportions of N counts found at each eyelid location. Because this model conditions on the total count $N (= Y_1 + Y_2 + Y_3 + Y_4)$, the parameters are necessarily restricted such that $1 = p_1 + p_2 + p_3 + p_4$. Therefore, only 3 of the parameters are free to be estimated; the fourth parameter is estimated by difference.

We used the method of maximum likelihood to estimate the parameters of these models from data. We also used likelihood-ratio tests to assess the significance of effects of covariates on N and to examine alternative hypotheses about the anatomical distribution of chalazia.

To examine the co-occurrence of internal and external chalazia, we compared the number of internal chalazia per eyelid for two groups of patients, those with one or more external chalazia and those without external chalazia. More specifically, we assumed the following model:

$$Y_{ij} \sim \text{Poisson}(\lambda_{ij})$$

where Y_{ij} denotes the number of internal chalazia on the j th eyelid location ($j = 1, \dots, 4$) of the i th patient. The parameter λ_{ij} denotes the number of internal chalazia that are expected on the j th eyelid of the i th patient given that external chalazia were present ($x_{ij} = 1$) or absent ($x_{ij} = 0$). Formally,

$$\log(\lambda_{ij}) = \beta_{0,j}(1 - x_{ij}) + \beta_{1,j}x_{ij}$$

This parameterization of the model implies that $\beta_{1,j}$ is the logarithm of the mean number of internal chalazia on the j th eyelid of patients with external chalazia. The parameter $\beta_{0,j}$ corresponds to the same quantity, but for eyelids without an external chalazion. We tested the null hypothesis that $\beta_{0,j} = \beta_{1,j}$ to assess whether numbers of internal chalazia depended on the presence or absence of external chalazia.

All the statistics were reported as 2-tailed probabilities, with P values < 0.05 being regarded as significant.

Results

A total of 128 consecutive children were included in the study. Revealing lymphohistiocytic granuloma with foam cells and foreign body giant cells, all the histopathological evaluations confirmed the diagnosis of chalazion.

The majority of children (74.2%) were under 3 years old, with a mean \pm SD age of 2.5 ± 0.9 years (range 1.0-6.5 years). The mean \pm SD disease duration was 2.2 ± 1.7 months (range 0.3-12.0 months). Fifty-seven patients were male (44.5%), 122 had bilateral lesions (95.3%), 127 presented internal chalazion (99.2%), 79 external chalazion (61.7%) and 3 marginal chalazion (2.3%). The mean \pm SD number of lesions per person was 8.30 ± 3.75 (range 2-22). Typical examples of multiple chalazia are shown in Fig. 1.

Distribution of internal chalazia

A negative binomial distribution with mean $\hat{\mu} = 7.42$ and overdispersion $\hat{\alpha} = 9.06$ provided a reasonably good fit to the observed numbers of chalazia ($P = 0.137$; Fig. 2). The mean \pm SD numbers of internal chalazia was 7.42 ± 3.73 (range 0-21). The total number of internal chalazia did not differ significantly with gender, age category, residence, or any combination of these covariates ($P = 0.073$; Table 1).

Estimates of the anatomical distribution of internal chalazia revealed a distinct pattern (Table 2), wherein the proportion of chalazia located on the upper eyelids was significantly higher than that of chalazia located on the lower eyelids ($P < 0.001$; Fig. 3), and there were more patients with chalazia on RUL (91.4%), followed by LUL, RLL and LLL (Fig. 4).

Distribution of external chalazia

A Poisson distribution with mean $\hat{\mu} = 0.875$ provided a reasonably good fit to the observed numbers of chalazia ($P = 0.383$; Fig. 2). The mean \pm SD numbers of external chalazia per person were 0.88 ± 0.87 (range 0-4). The total number of external chalazia did not differ significantly with gender, age category, residence, or any combination of these covariates ($P = 0.280$; Table 1).

There were more patients with one or more external chalazia than those who had none (61.7% vs 38.3%; Fig. 2). Among the former group, at most 3 separate lids were involved by external chalazia, and 1 lid involvement was most common (39.1%). The majority of patients in our study had no more than 1 external chalazion on each separate eyelid, except for 1 case that presented 2 external chalazia on 1 eyelid. Estimates of the anatomical distribution of external chalazia revealed no significant differences among eyelid locations ($P = 0.581$; Fig. 3), and there was no difference between the 4 lids with respect to the proportion of patients with external chalazion (Fig. 4).

Co-occurrence of internal and external chalazia

The abundance of internal chalazia did not depend on the occurrence of external nodules ($P = 0.424$). To be more specific, in each eyelid the mean number of internal chalazia did not differ significantly between eyelids with external chalazia and those without ($P = 0.177, 0.179, 0.292, 0.769$ for RLL, LLL, RUL, and LUL, respectively). This result is evident in Fig. 5.

Discussion

In the present study, we demonstrated that multiple chalazia that need surgical treatment were more common in younger Chinese children (aged 1 to 3 years). The mean number of lesions per person was 8.3. Internal chalazion was the most common type, external chalazion occurred in more than half of the patients, and marginal chalazion was rarely observed. In addition, the abundance of internal chalazia in upper lids was higher than that in lower lids, whereas the abundance of external chalazia was similar in each eyelid.

Arie demonstrated a high incidence of chalazion in people from urban areas and in females from 10 to 29 years of age [19]. In our study, the majority of subjects were pre-schoolers, and multiple chalazia were more common in children aged 1 to 3 years than those aged 3 to 7 years; however, the abundance of multiple chalazia did not differ with gender, age category, or residence groups. Lin C found that children aged 6 months to 6 years usually had more chalazia than older children (7 to 12 years of age) [5]. Wagner reported that children transferred to ophthalmologists with multiple and bilateral chalazia were often between 3 to 5 years old [4]. The risk factors leading to multiple chalazia in young children are unclear, and low serum vitamin A might be one [5].

The anatomical distribution of internal chalazia correlates with the characteristics of meibomian glands. Shirakawa R studied the meibography of Japanese children (aged 1 month to 12 years) and found numbers of meibomian glands in the upper and lower tarsal plates were approximately 26.9 and 22.0, with no significant statistical difference [20]. However, the upper lid had much denser, thinner and longer meibomian glands [20, 21], which are supposed to be the main anatomical traits responsible for the higher numbers of internal chalazia in upper eyelids. Thus far, no publications have reported a definite difference of abundance of internal nodules between upper and lower lids. However, in our study bilateral upper lids presented 1.4 times more internal lesions than the lower lids.

Compared to internal chalazia, the proportions of patients with external and marginal chalazia were lower (99.2% vs. 61.7% and 2.3%), the number of external lesions per patient was smaller (7.4 vs. 1.0), and the anatomical distribution of external type showed no difference between the lids ($P < 0.001$ vs $P = 0.581$). Little information is available on the precise number of zeis glands; however, given that the zeis gland opens into eyelash follicles and that there are more upper eyelashes than lower eyelashes [22], we speculate that more zeis glands should also be present in the upper lids. However, the anatomical distribution of external or marginal chalazia totally differs from that of internal lesions. There could be 3 possible explanations for this difference: (1) compared to the meibomian gland, the zeis gland is less likely to be plugged due to its shorter duct [23]; (2) the sebum secreted by the zeis gland can inhibit

bacteria [24], which may play a role in chalazion formation [25, 26]; and (3) being thicker and stronger than conjunctiva, skin is more difficult for lumps to penetrate.

To our knowledge, the relationship between internal and external chalazia has not previously been reported. Sometimes an external chalazion comes from a growing internal chalazion that penetrates the tarsus and appears superficial on the skin. This can be proven by the hole through the tarsal plate after the removal of a chalazion. However, in our study no relationship was discovered between these two types of chalazia for each separate lid, which could indicate that the formation of internal and external chalazia is relatively independent.

Although our study provides the first detailed examination of the anatomical distribution of multiple chalazia in children of Zhejiang, China, some limitations should be considered. First, all the patients in our study came from one hospital in southeast China, and they all needed I&C operations. The patients that did not receive surgery, such as those with very small nodules or with short clinical courses, or the infants whose parents were concerned about the safety of systemic anesthesia or surgery, may not be included in our study, thus resulting in a selected population. Second, cases with 2 or more external chalazia on one lid were quite rare in our study, possibly because of relatively short research time or the parent's desire for early treatment due to a cosmetic problem. Third, we did not assess whether the chalazion was located in the medial, central or lateral eyelid, because this classification can be subjective if the nodule is large in size. In future studies, a multi-centered approach with a longer observation time and with patients of a greater range of ages could provide additional information about the anatomical distribution of multiple chalazia.

Conclusions

Among the children who needed I&C surgery in Zhejiang province, multiple chalazia were more common among patients aged 1 to 3 years old. Multiple chalazia often occurred bilaterally and were more abundant in the upper eyelids; however, different types of chalazion presented different distributions. External chalazia are obvious and doctors are more likely to detect them than other types of chalazia. However, because bilateral and internal chalazia are quite common, everting the other eyelids to check for internal lesions should be emphasized in surgery. Our study provides a deeper understanding of the anatomical distribution of multiple chalazia in pediatrics and its implications for treatment.

Tables

Table 1 Demographic distributions and different types of chalazia

| | Chalazion | | Internal chalazion | | External chalazion | |
|------------------|----------------|----------------|--------------------|----------------|--------------------|----------------|
| | N _p | N _n | N _p | N _n | N _p | N _n |
| Age | | | | | | |
| <3 years | 95(74.2) | 8.39±3.52 | 94(73.0) | 7.57±3.49 | 57(72.2) | 0.82±0.85 |
| >=3 years | 33(25.8) | 8.03±4.38 | 33(25.9) | 7.00±4.37 | 22(27.8) | 1.03±0.92 |
| Gender | | | | | | |
| Male | 57(44.5) | 7.65±3.58 | 56(44.1) | 6.89±3.57 | 32(40.5) | 0.75±0.81 |
| Female | 71(55.5) | 8.82±3.83 | 71(55.9) | 7.85±3.82 | 47(59.5) | 0.97±0.91 |
| Residence | | | | | | |
| Downtown | 69(53.9) | 8.41±4.13 | 69(54.3) | 7.57±3.99 | 45(57.0) | 0.84±0.74 |
| Countryside | 59(46.1) | 8.17±3.29 | 58(45.7) | 7.25±3.42 | 34(43.0) | 0.92±1.00 |
| Total | 128(100) | 8.30±3.75 | 127(99.2) | 7.42±3.73 | 79(61.7) | 0.88±0.87 |

N_p number of patients presented as number (% of total), N_n number of nodules presented as mean ± SD

Table 2 Details of lid distributions with respect to different chalazion types

| Location | Internal chalazion | | External chalazion | |
|----------|--------------------|----------------|--------------------|----------------|
| | N _p | N _n | N _p | N _n |
| RUL | 117(91.4) | 2.18±1.36 | 30(23.4) | 0.24±0.45 |
| RLL | 101(78.9) | 1.45±1.11 | 30(23.4) | 0.23±0.43 |
| LUL | 111(86.7) | 2.11±1.51 | 27(21.1) | 0.21±0.41 |
| LLL | 99(77.3) | 1.68±1.44 | 24(18.8) | 0.19±0.39 |

N_p number of patients presented as number (% of total)

N_n number of nodules presented as mean ± SD

Abbreviations

RUL: Right upper lid; LUL: Left upper lid; RLL: Right lower lid; LLL: Left lower lid; I&C: Incision and curettage; SD: Standard deviations

Declarations

Acknowledgements

Not applicable.

Authors' contributions

XZ contributed in conception and design and writing the manuscript, RD contributed in analysis and interpretation of data, TW and SZ contributed in acquisition of data, ZZ contributed in supervision. The authors read and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

All procedures performed in studies involving human participants were in accordance with the ethical standards of Institutional Ethics Committee of Children's Hospital Zhejiang University School of Medicine and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards (No. 2018-IRB-041). Informed consents were obtained from the parents whose child's photos were taken.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Figures



Figure 1

Typical manifestation of multiple chalazia in children. Arrows indicate the internal nodules, arrow heads indicate external lesions, and asterisk indicates marginal chalazion.

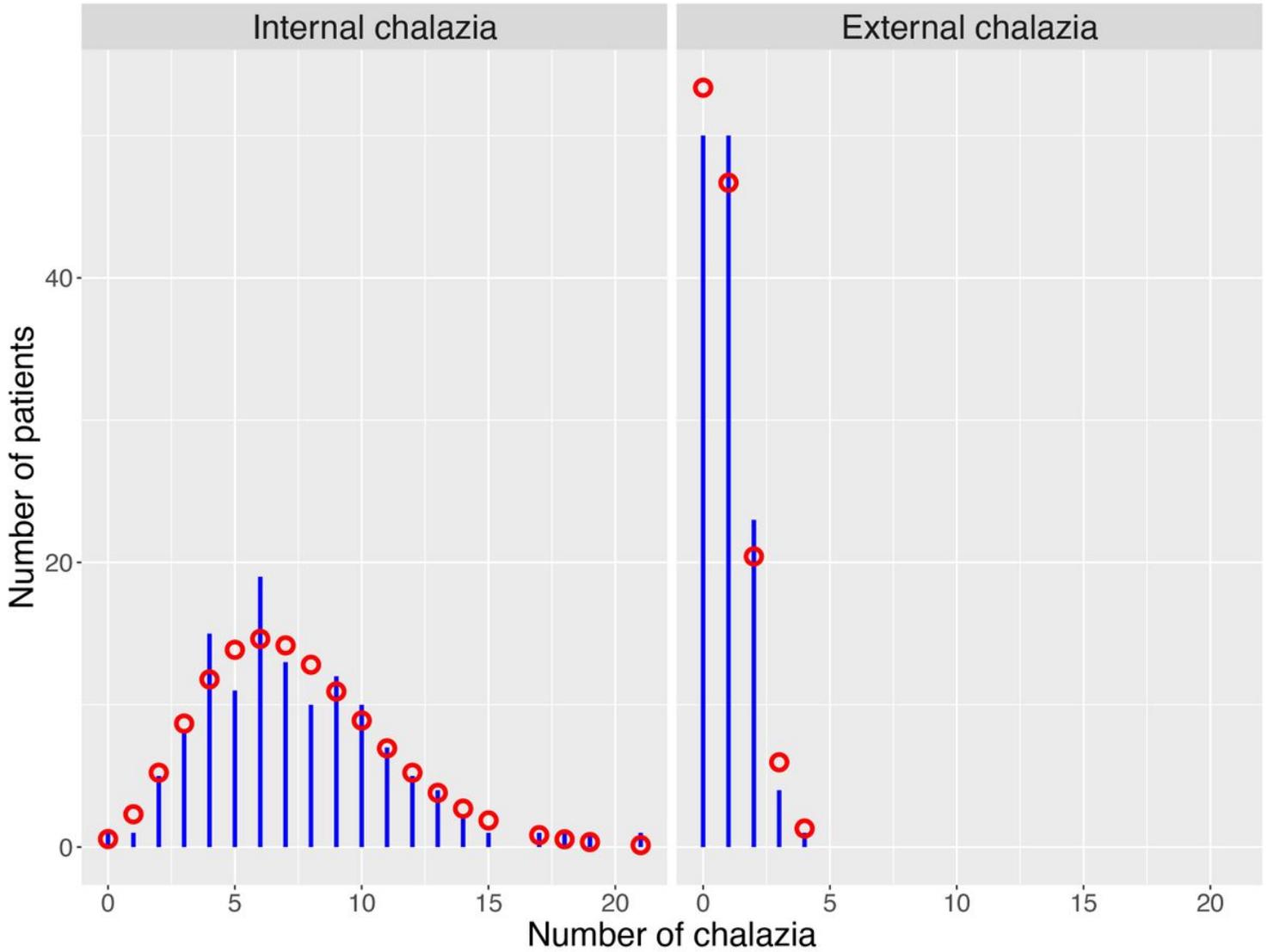


Figure 2

Distributions of the total number of chalazia observed among 128 patients. Circles indicate the expected numbers of chalazia based on the fit of a negative binomial model (internal chalazion) or a Poisson model (external chalazion).

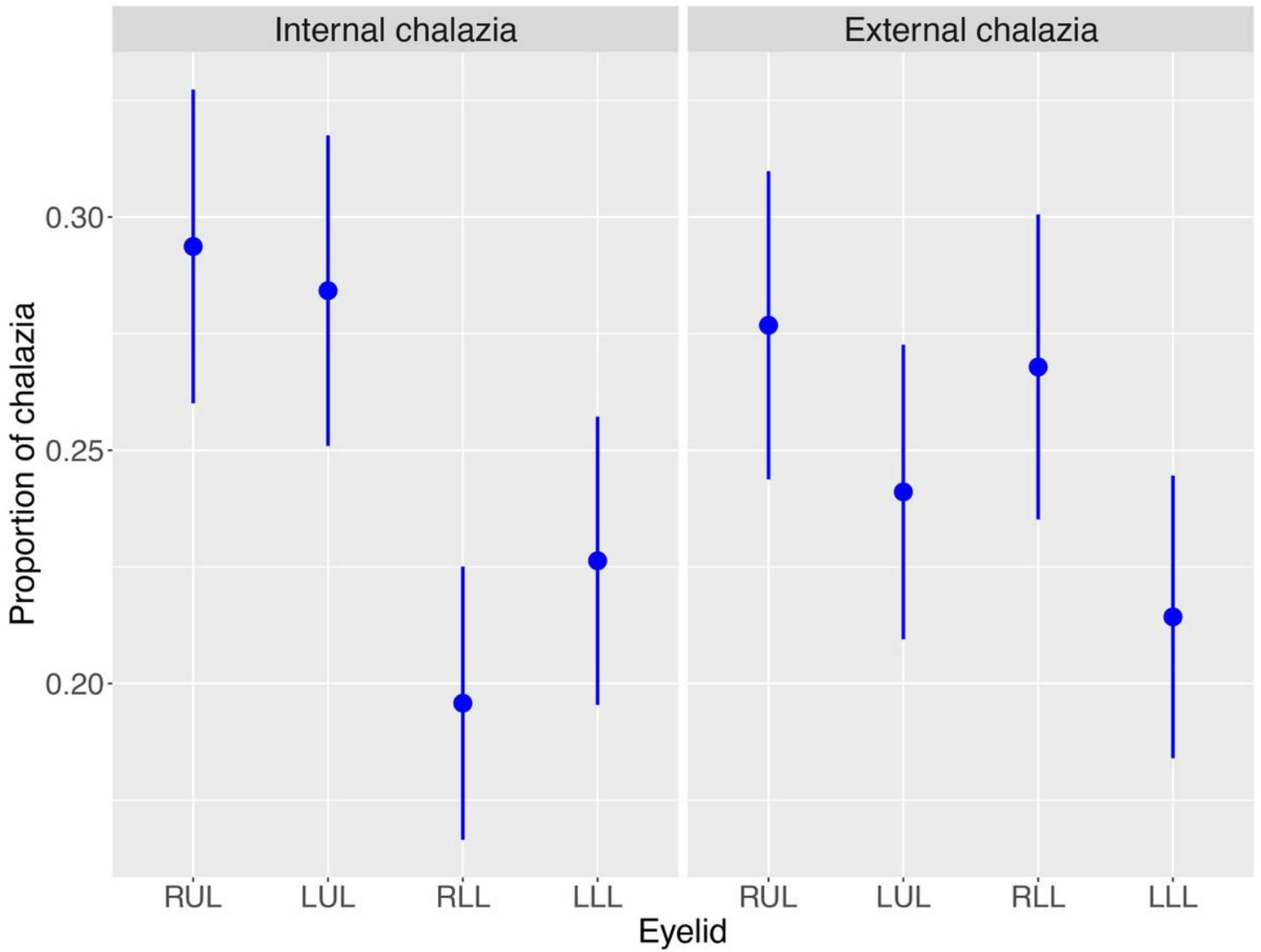


Figure 3

Estimates (with 95% confidence intervals) of the anatomical distributions of internal and external chalazion

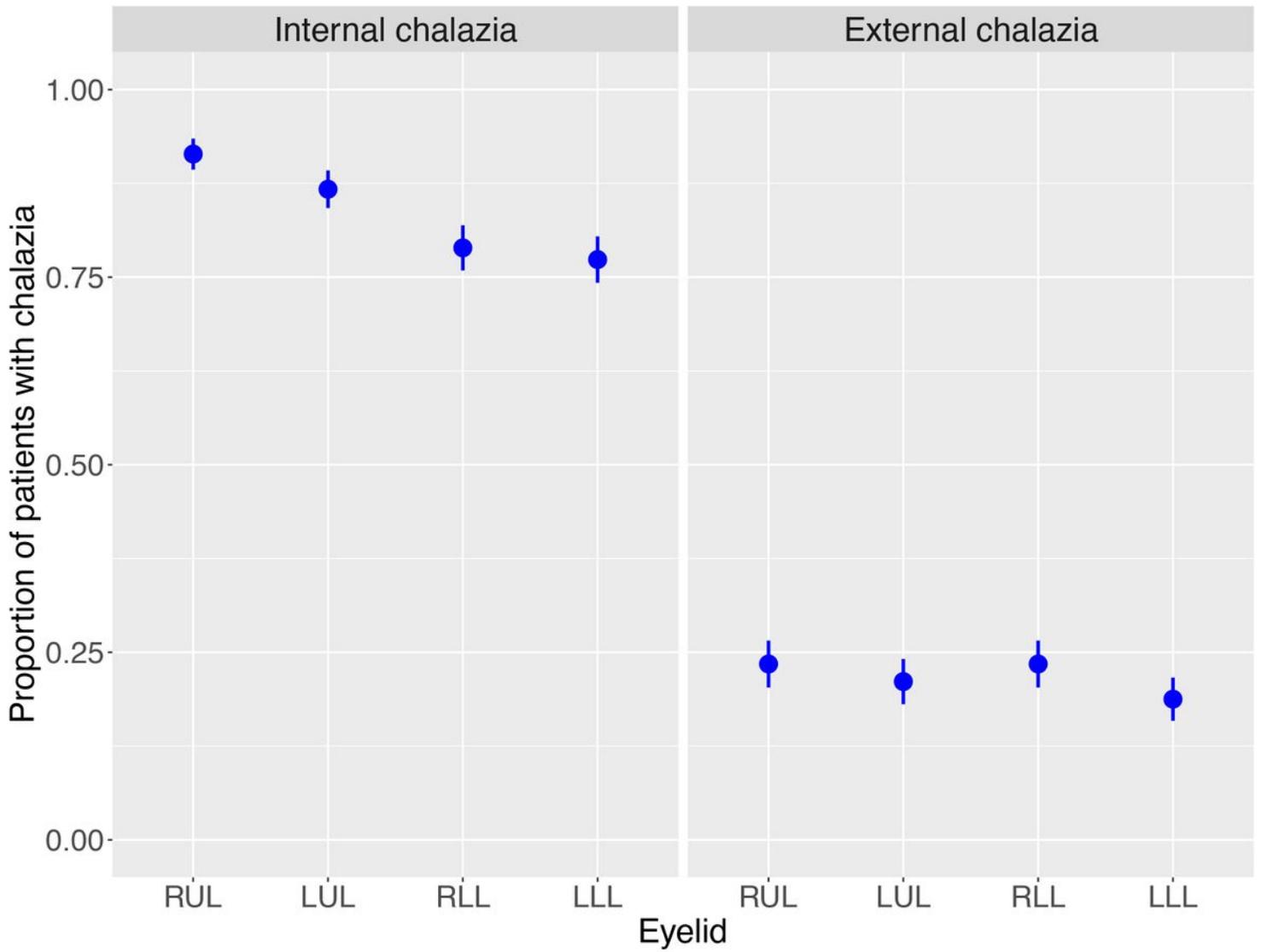


Figure 4

Estimates of the proportion of patients with internal and external chalazion.

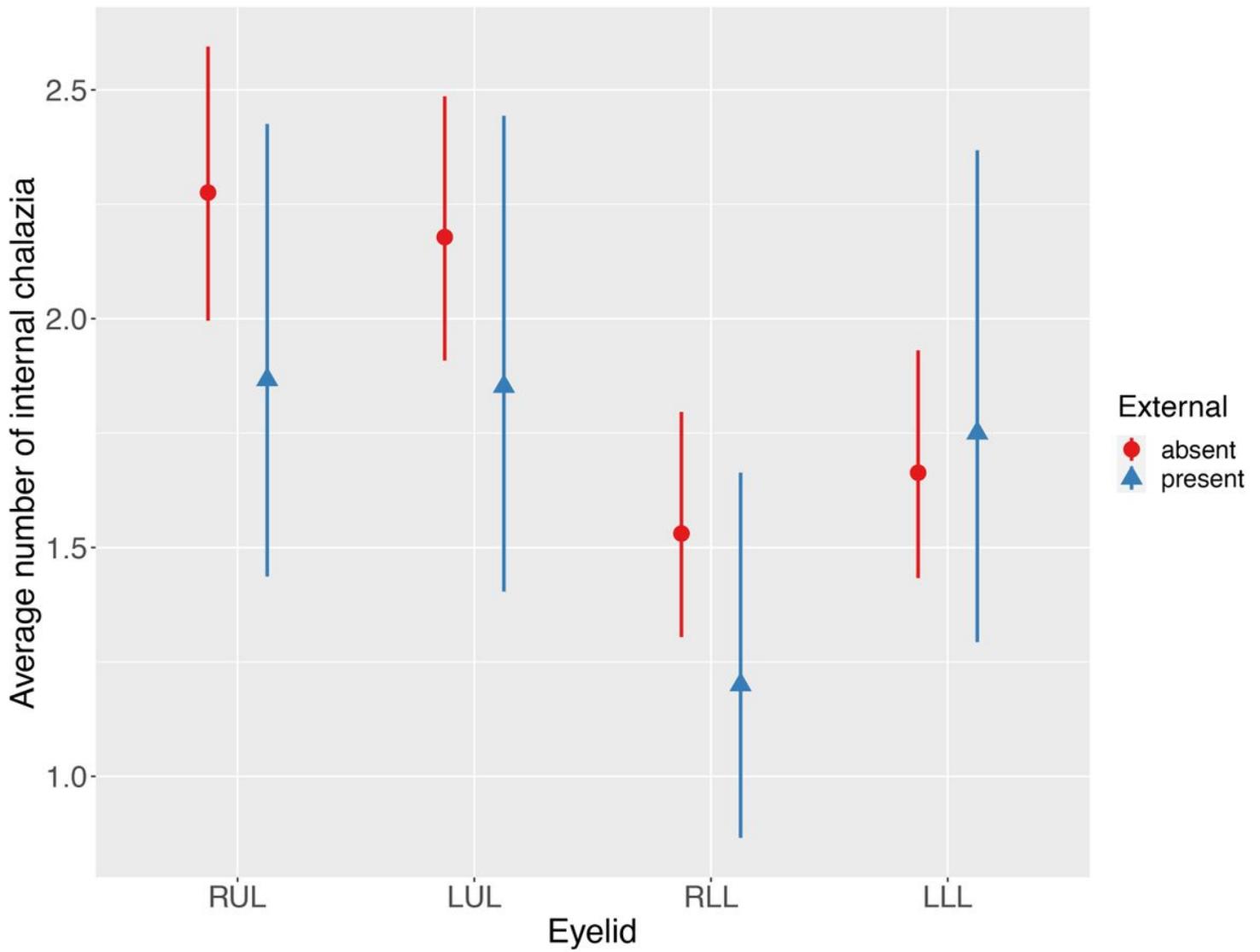


Figure 5

Estimates (with 95% confidence intervals) of the average number of internal chalazion on eyelids where external chalazion were absent (red circle) or present (blue triangle).