MEDICAL UNIVERSITY PLEVEN
DEPARTMENT „OPHTHALMOLOGY, ENT DISEASES,
MAXILLOFACIAL SURGERY WITH SURGICAL DENTISTRY”

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EYELID TUMORS

ABSTRACT

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The dissertation work was examined, discussed, and directed for a public defense to an extended departmental council at the Department of Ophthalmology, ENT, MFS with SD at Medical University - Pleven.
The dissertation student works in the same department at UGHAT "G. Stranski" - Pleven.

USED ABBREVIATIONS

BCC – basal cell carcinoma
SCC – squamous cell carcinoma
SGC – sebaceous gland carcinoma
MM – melanoma malignum
NSI – National Statistical Institute
WHO – World Health Organization
UGHAT – University General Hospital for Active Treatment
HPI – History of the patient's illness
M/B/I – Malignant / Benign / Inflammation

The numbering of the figures does not match that in the dissertation.

The public defence of the dissertation work will take place on 16.05.2023 at 11:30 o'clock at II-nd Clinical Base, Parvum Hall.
The defense materials are available on the website of the Medical University of Pleven, as well as in the secretariat of the University.

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INTRODUCTION

Healthy cells change under the influence of various factors and begin to grow uncontrollably, which leads to the formation of a mass of tissue called a tumor. Malignant tumors grow and spread to other organs and tissues, while benign tumors only grow without spreading.

The eyelids are a small organ, part of the accessory structures of the eye; nevertheless, they contain several histological layers from which both benign and malignant tumors can originate. Their skin is the thinnest and most sensitive part of the human body's skin. The eyelids, compared to other parts of the face, are often the first place where neoplasms or disease changes are noticed.

These lesions are one of the frequent reasons for visiting an ophthalmologist. The treatment is mainly surgical and aims to preserve the anatomical structure of the eyelid, its function and last but not least, its aesthetic appearance. The postoperative result should largely meet the patient's cosmetic expectations. This implies a well-prepared surgical team and early operative intervention. On the other hand, long-standing tumors involve large areas of the eyelid tissues and make the surgical outcome unpredictable.

Eyelid surgery is part of oculoplastic surgery, which is a division of aesthetic surgery. It requires combining general surgical with aesthetic principles in order to achieve a good result. In this scientific work a broad overview of operative techniques, instrumentation, suture material is made. Major surgical complications and their treatment are also discussed.

AIMS AND TASKS

Aim: To make a retrospective assessment of the frequency, histological variants, and the results of reconstructive methods in the treatment of tumors of the eyelids for ten years in patients of the Ophthalmology Clinic - Pleven.

Tasks:

1. To analyze the frequency of eyelid tumors – according to materials of the Pleven Ophthalmology Clinic for the period 2010-2019.
2. To compare the frequency of tumor diseases with other authors for a similar period.
3. To analyze the histological variability of eyelid tumors for the considered period.
4. To analyze the operative technique for the different groups of reconstructive procedures.
5. To evaluate the functional and cosmetic result of the surgical treatment, as well as the possibility of its optimization.

MATERIALS AND METHODS

CLINICAL MATERIAL

A retrospective clinical study was conducted in which 436 patients with eyelid tumors in 450 surgeries were followed and analyzed. All cases were operated on in the ophthalmology clinic at the UGHAT "Dr. G. Stranski" - Pleven. The presented results are only from well-documented cases for a ten-year period of clinical observation /2010-2019/. Patients were stratified by sex, age, histology, location, size, ciliary margin involvement, and surgical procedure.

To develop a patient database, the following information was collected: the medical documentation from the patient's stay - HPI, operative protocols, histological protocols, documentation from control

examinations, photo-documentation of operations and control examinations, other medical documentation.

METHODS

All patients underwent a general medical examination (clinical minimum laboratory tests, consultative examination with an internist, anesthesiologist) and a complete ophthalmological examination.

OPERATING TECHNIQUE

Surgeries were performed under general and local (conductive or infiltrative with or without akinesia with 2% lidocaine) and, if necessary, retrobulbar. In cases with local anesthesia, additional premedication was carried out. In individual cases, local anesthesia is combined with intravenous (propofol).

Excision of the tumor was done in full or partial thickness of the eyelid. The next step is reconstruction of the defect, where the following surgical techniques are applied: 1. Laissez-Faire; 2. Direct closing; 2. Reconstruction with different types of flap; 3. Free skin graft; 4. Glabellar plastic; 5. Other reconstruction.

In some cases, the surgery was performed in 2 stages. In the first stage, excision of the tumor was performed, and in the second stage, reconstruction of the defect. The second stage was performed after obtaining the histological result - on average 7 days.

The postoperative period is divided into two periods: early postoperative period: the time from surgery to the 7th day. In this period, we monitor for: inflammatory reactions, loosening of the sutures with wound dehiscence, necrosis of the transplant and the lamp. The late postoperative period lasts from the removal of the sutures on the 7th day to the first month. During this period, the patient is observed frequently,

the characteristics of scarring and positional abnormalities are monitored. For malignant tumors, follow-up lasts three years (1, 3, 6 months, etc.), during which the recurrence of the main tumor at the edges of the wound is monitored.

STATISTICAL METHODS

Survey data were processed with SPSS and EXCEL. A descriptive analysis was performed, and the normal distribution of the parameters was checked with the Kolmogorov-Smirnov and Shapiro-Wilk tests. In the variance analysis, parametric tests for testing hypotheses such as: t-test, ANOVA with post-hoc tests, Tukey, etc. were applied. Non-parametric tests for different from the normal distribution of cases are: Pearsonχ^2 - test, Mann-Whitney, etc. The significance of the conclusions was determined by the Pearson coefficient at a significance of $p < 0.05$.

RESULTS

STATISTICAL ANALYZES

DESCRIPTIVE ANALYSIS

The retrospective study included 450 surgeries in 436 patients. The distribution of tumors according to their histology was examined within the group as follows - malignant (21.3%), benign (71.8%), inflammatory (6.5%), and least precancerous (0.4%) (Figure 1).

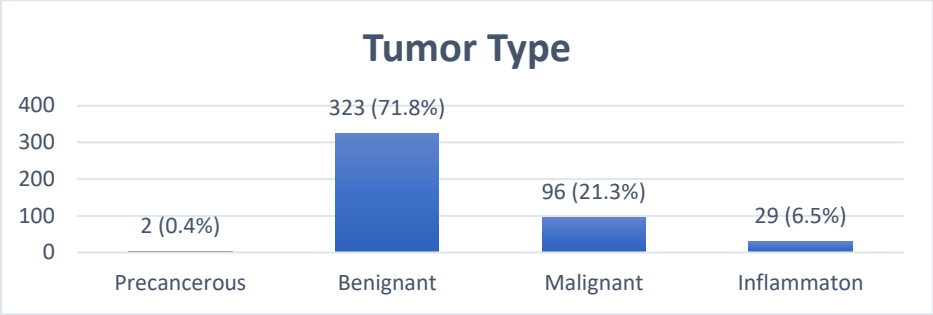


Figure 1. Distribution of tumors by number

Among malignant tumors, the first place is the basal cell carcinoma (BCC) 71.9%, followed by the squamous cell carcinoma (SCC) – 16.7% and the third place is the sebaceous carcinoma (SGC) – 4.2% (Figure 2).

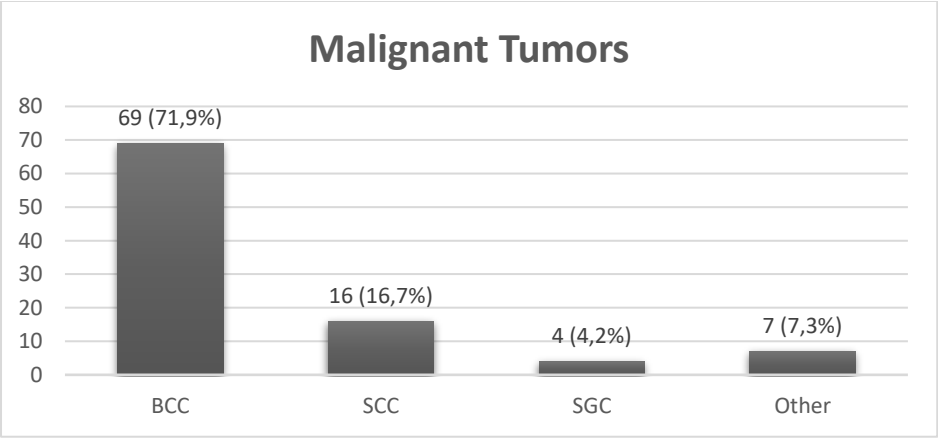


Figure 2. Distribution of malignant tumors according to histology

In benign tumors, the distribution was: cysts (38.8%), papillomas (27.4%), nevi (10.2%), keratoses (7.4%), hemangiomas (4.3%) and others (Figure 3).

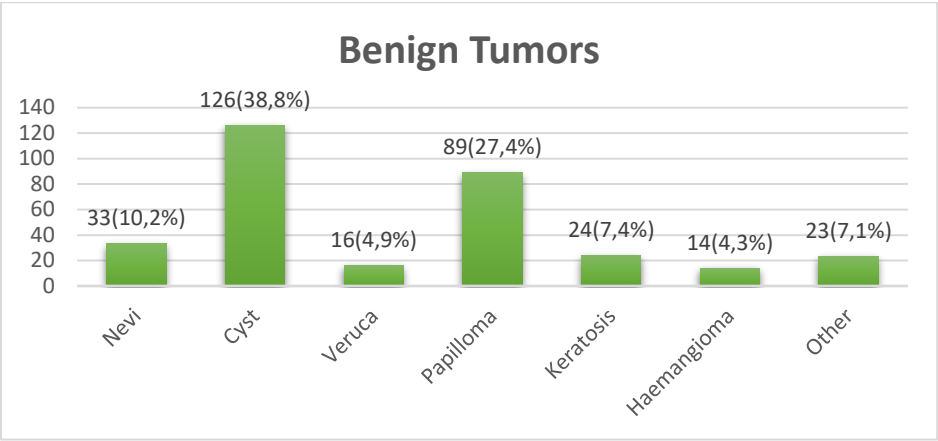


Figure 3. Distribution of benign tumors according to histology

Inflammatory diseases were diagnosed primarily as a tumor, accounted for 6.5% of all cases, and did not include chordeolum. Their histology shows cells of inflammation, mycosis, virosis, etc.

The gender distribution of patients was 57% (255) female to 43% (195) male. According to tumor histology, similar results were observed: benign tumors - 57% (201) women and 43% (154) men; malignant tumors – 57% (54) women to 43% (41) men. No significant difference was found regarding gender and malignancy (p=0.97) (Figure 4).

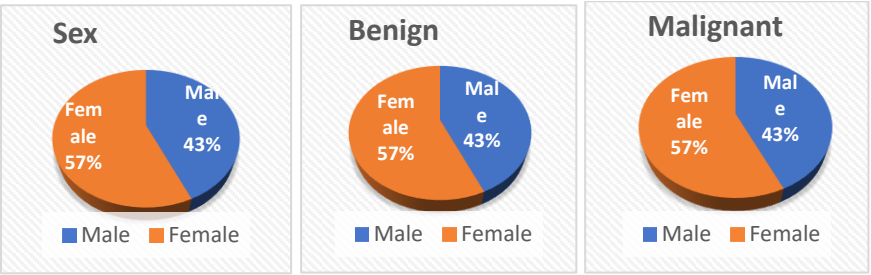


Figure 4. Distribution by A-sex, B-benign, C- malignant tumors

The age indicator is divided into 7 subgroups as shown in the graph (Figure 5).

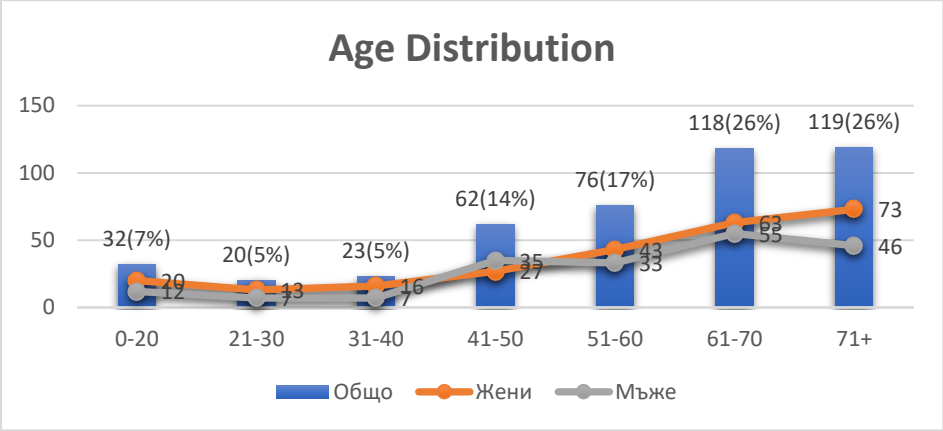


Figure 5. General age distribution of all tumors by sex

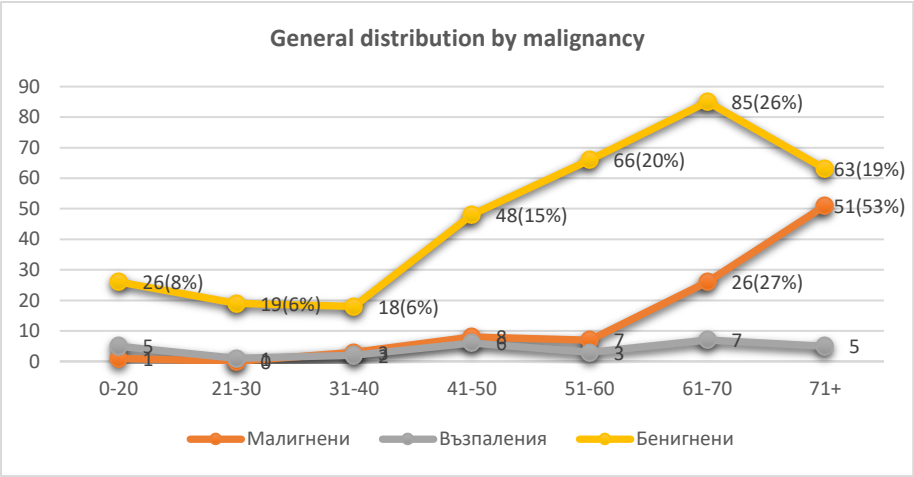


Figure 6. General age distribution of malignant, benign and inflammatory tumors

The mean age is 57.39 years (the median is 62 years - the same for men/women, and the mode is 70 years). Most tumors are in the group after 60 years of age. From the statistical analysis, it can be seen that age and malignancy are in a positively significant relationship ($\chi 2=60.78$, df=12, p>0.001, ETA=0.20), it means that the two indicators increase together.

The overall distribution of tumors by age and malignancy is presented in **Error! Reference source not found.**6. The increase in the total number o f tumors begins after the age of 40 at the expense of benign tumors - a total of 14%. Up to the age of 60, the growth of tumors is mainly at the expense of benign ones. In the period of 60-70 years, in addition to the benign ones, the malignant ones also started to increase, but the greater percentage falls on the benign ones. From the age of 70 onwards, malignant tumors increase several times and represent the following ratio: benign - 53%, malignant - 43%, inflammation - 4%.

In the case of malignant tumors over 60 years of age there is a threefold increase compared to the previous groups, and over 70 – a sixfold increase. We can formulate a positively significant relationship starting from the age of 31-40, where they are about 3%; at 61-70, the percentage reaches 27%, and the over 71 group is 53%.

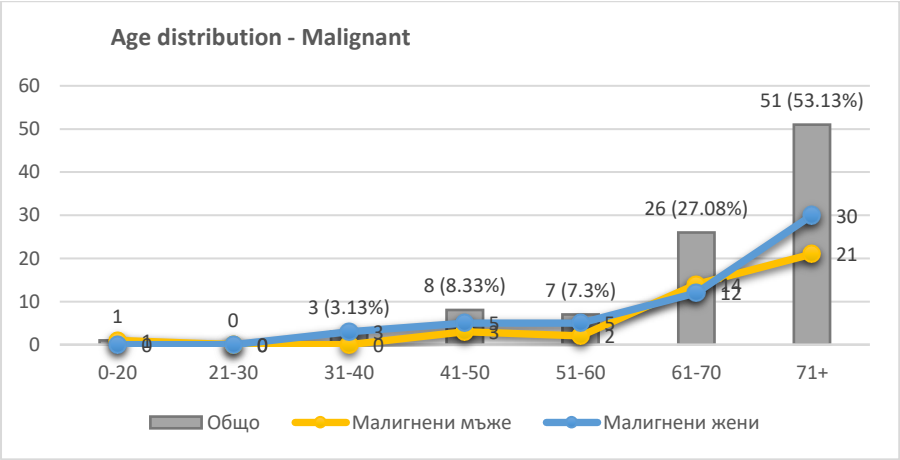
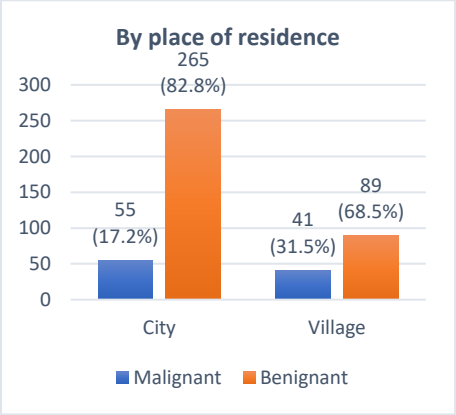


Figure 7. Age distribution in the group of malignant tumors

In benign tumors, a small peak is observed in the group 0-20 years, but after 40 years, a marked increase in cases begins, which continues until 70 years, after which we observe a marked depression. Graphs of the age distribution of tumors, overall and intra-group, are left skewed.

Inflammatory diseases show a relatively even distribution without significance in the individual groups.

The incidence by gender is similar in men and women up to age 70. After the age of 70, it is observed that the graph of women for malignant tumors stands above that of men and is in the ratio of 59%(F) to 41%(M), but no intergroup difference was found (Figure 7). Overall, for the three groups (malignant, benign, and inflammatory), when distributed by sex, no significant intergroup differences were found, and it can be assumed that we have an equal distribution by gender.



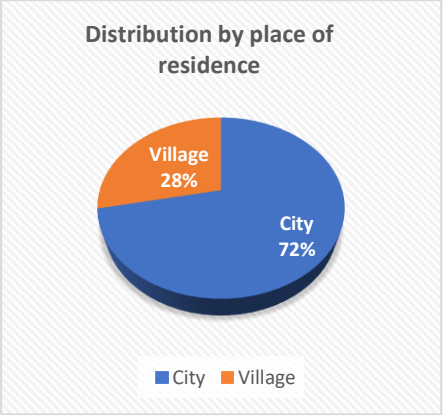


Figure 8. Analysis by place of residence

Figure 9. Distribution by place of residence

The incidence according to place of residence shows a high significant dependence of malignant cases in favor of the group living in villages, in contrast to benign cases in the group living in cities, where they prevail ($\chi 2=11.65$, df= 2, $p<0.001$, Eta=0.161) . Malignant cases in villages represent 31.5% compared to those in cities – 17.2%, and benign cases show the reverse ratio – 68.5% in villages and 82.8% in cities (Figure 8,9).

The distribution by place of residence shows an advantage for those living in the city, but after a cross-analysis by place of residence and age, it is found that the older population (60+ years) lives mostly in villages ($p<0.002$).

Statistical descriptive analysis based on occupation showed a significant difference between the "worker" and "retired" groups for both malignant and benign tumors ($p<0.01$). The ratio in pensioners is 32% for malignant

to 68% for benign. Division of eyelid tumors according to facial symmetry (left/right eye) showed no significant difference (p=0.19).

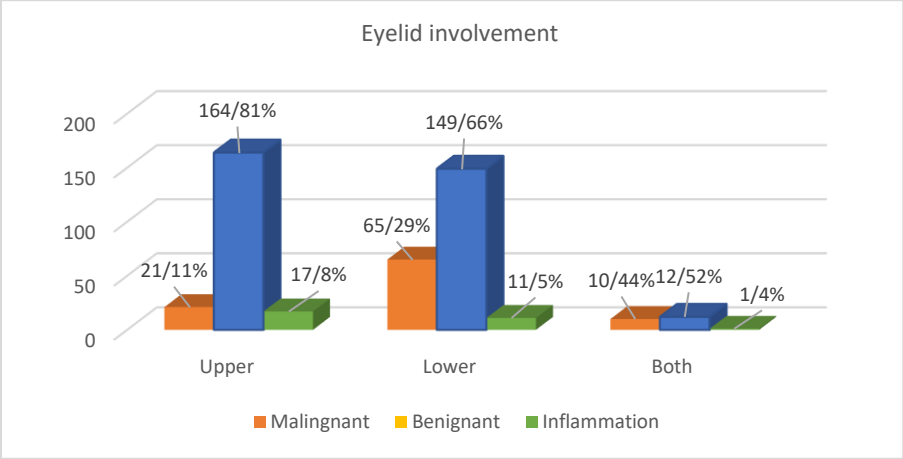


Figure 10. Localization according to the eyelids

In total, the tumors were distributed according to the involvement of upper – 202 (45%), lower – 225 (50%), and both eyelids – 23 (5%). Of these, 96 (21.3%) were malignant, 325 (72.2%) were benign, and 29 (6.4%) were inflamed (Figure 10). From the statistics made, it is found that the lower eyelid is preferred by malignant tumors, compared to the upper one in the ratio of 67.7% to 21.9%, and 10.4% are cases with two eyelids involved. Benign tumors are equally distributed between the lower and upper eyelids with a slight preponderance towards the upper: 50% to 45% (5% inflammatory). Involvement of both eyelids at the same time is in equal proportions, but with a slight preponderance in favor of benign - 44% to 52% (2% inflammation) ($\chi 2=29.51$, df=4, $p<0.001$, Eta=0.255). On the other hand, the intra-group recalculation of percentages is as follows: upper eyelid (M/B/I – 10.4%/81.2%/8.4%), lower eyelid (M/B/B –28.9%/66.2%/4.9%), both (M/B/B – 43.5%/52.2%/4.3%) (Figure 10).

Each eyelid was conditionally divided into 3: nasal, central, and temporal localization, and for tumors covering both eyelids, the areas involving

the medial and temporal canthus, were added. These groups were compared separately for malignant and benign tumors and inflammation.

In malignant tumors, the distribution is in favor of the lower eyelid. The percentage ratio of the three parts of the lower eyelid is nasal - 36.9%, central - 41.5%, and temporal - 18.5% ($\chi 2=41.45$, df=8, $p<0.001$). The upper eyelid was involved nasally in 23.8%, centrally in 57.1%, and temporally in 4.8%. Regarding the temporal and medial canthal areas, the distribution is significantly skewed in favor of the medial canthal, 80% to 20%. Cases with medial or temporal eyelid involvement and canthus involvement are referred to as the medial and temporal canthus, respectively, and are not part of the above percentages.

In benign tumors, the distribution according to the localization of the defect shows a relatively equal ratio - 50% to 45%, relative to the upper and lower eyelid. The medial canthal area is preferred over the lateral one in a ratio of 66% to 42% ($\chi 2=28.35$, df=16, $p<0.029$). The rest of the specifications are in a similar percentage ratio as for the malignant ones, but do not have great significance ($\chi 2=10.02$, df=8, $p>0.26$).

The total number of inflammations is small to make meaningful statistics, but based on the available data, we can conclude that the upper eyelid is a preferred location in 58.6% compared to 37.9% for the lower. The distribution between the medial, middle and temporal 1/3 of the eyelid, in inflammations, is in favor of its middle part ($\chi 2=2953$, df=6, $p<0.001$), but there are no significant differences between the upper and lower eyelid.

Tumors in the area of the eyelid margin was observed in 134 cases - 39 malignant, 88 benign and 7 inflammations. Of these, the cases with full-thickness involvement of the lash line were 35. 29 (83%) were malignant, and 6 (17%) were benign (Figure 11). The relationship between eyelid margin involvement and tumor malignancy showed a statistically significant relationship with a large weight coefficient ($\chi 2=89.72$, df=2 , $p<0.0001$, Eta=0.390) (Figure 11).

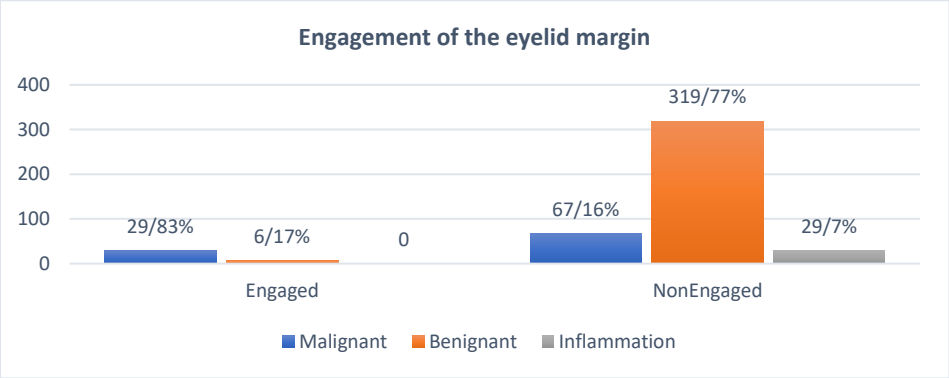


Figure 11. Engagement of the eyelid margin

We analyzed eyelid margin involvement by age and observed a significant difference, especially for the 61-70 years and 71+ years groups, representing 20% and 60% of all cases with eyelid margin involvement ($\chi 2=23.49$, df=6, $p<0.001$).

Another analysis we performed looked at cases with involvement of the eyelid margin in combination with a clinically visible inflammatory reaction of the eyelid skin around the tumor (25.7%), especially that near the lash margin (42.9%), as well as in combination with involvement on the medial canthus (14.3%). We observed a statistically significant dependence ($\chi 2=39.71$, df=5, $p<0.001$). The combination of involvement of the ciliary margin, skin near the eyelid margin, and/or the medial margin increases the likelihood of malignancy many times over.

The canthal area was involved in 25 cases. The ratio is 65.4% medial to 34.6% temporal. This ratio was similar for both benign and malignant tumors ($\chi 2=1.98$, df=2, $p>0.37$), making the medial canthus the preferred location for all tumors, not just malignant ones (Figure 12).

The inflammatory reaction of the surrounding tissues (without involved eyelid margin) in malignant tumors represents 48.1%, in benign tumors - 34.2%, and in inflammations - 17.7%. The absence of inflammatory reaction of the surrounding tissues was distributed 15.6%/80.3%/4% for malignant/benign/ inflammation ($\chi 2=70.3$, df=2, $p<0.001$).

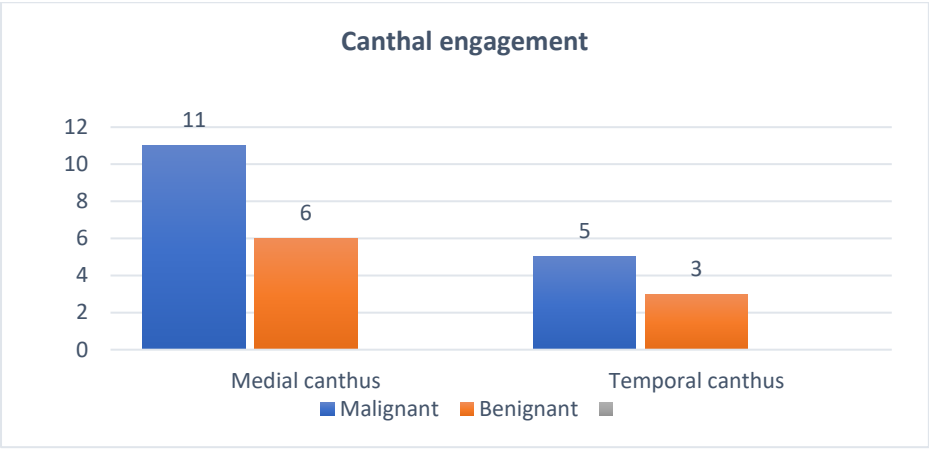


Figure 12. Correlation between the medial and temporal canthus.

According to tumor size, patients were divided into five groups – 0-3 mm, 4-6 mm, 7-10 mm, 11-15 mm, and 15+ mm (Figure 13). The size does not always correspond to the histology, but statistically, it was found that small sizes are characteristic of benign tumors and inflammations, while large sizes are characteristic of malignant tumors ($\chi 2=53.75$, df=8, $p<0.001$).

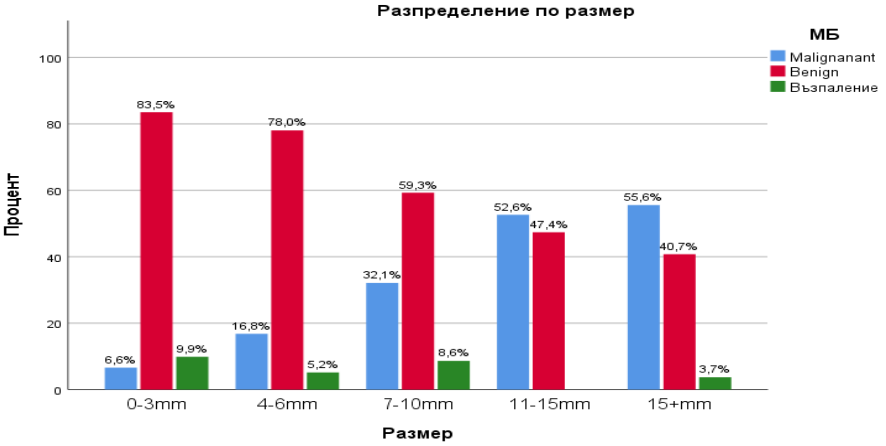


Figure 13. Distribution by size and type.

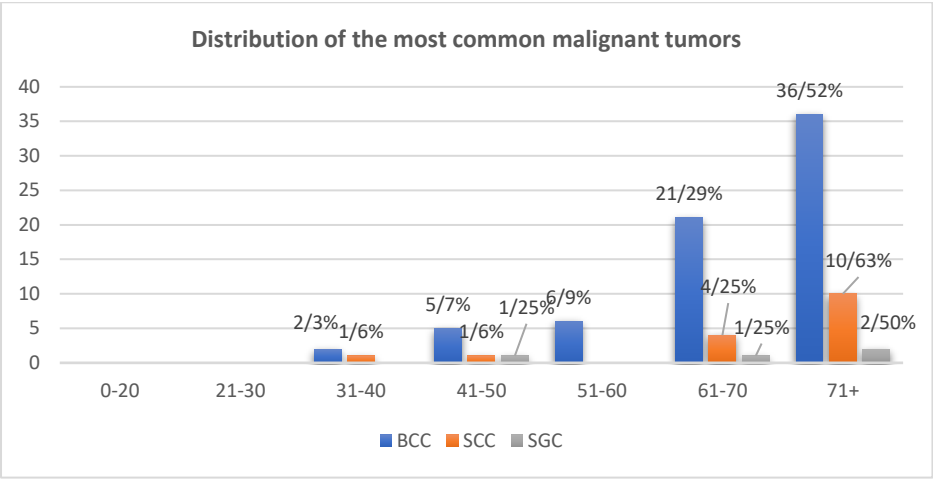


Figure 14. Distribution of the most common malignant tumors by age

At sizes of 7 mm and above – the statistical distribution is in favor of malignant tumors. The statistical test determining the significance of the distribution is highly important (ETA= .330). In the groups above 11 mm, malignant tumors prevail.

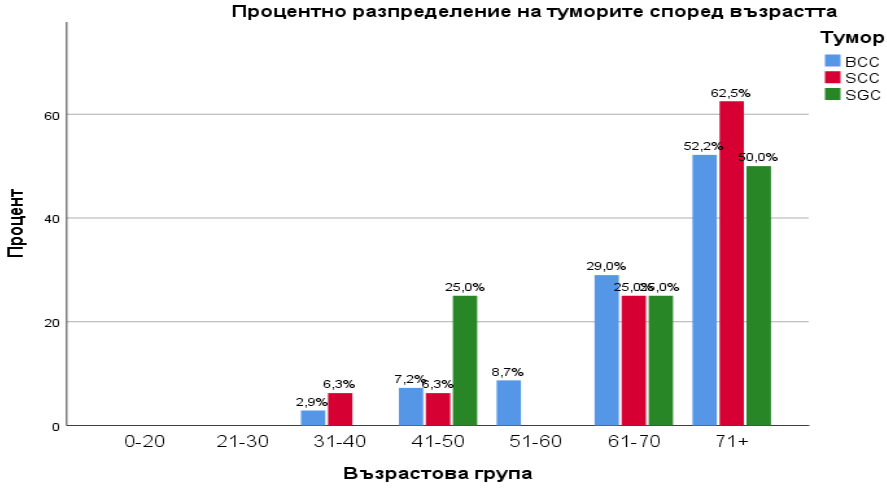


Figure 15. Percentage distribution of the most common malignant tumors by age

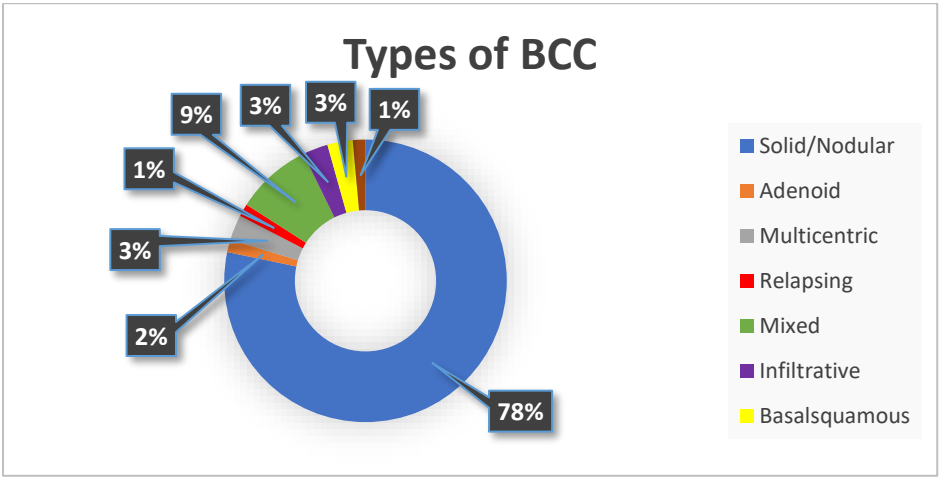


Figure 16. Distribution of BCC histological types

The distribution by the morphology of the most common tumors according to age can be seen in Figure 14. For all ages, the highest percentage is BCC, but SCC and SGC, despite their small numbers, show an increase in two age groups, which is seen better on the graph with the percentage distribution in Figure 15. Up to 40 years of age, the frequency of malignant tumors is relatively small - 4.2%; from 40 to 60 years is 15.6%; after 60 years, it is (27.1%); and after 71 years, it is (53.1%). The distribution between the histological variants of the malignant tumors was: BCC – 71.9%, SCC – 16.7%, SGC – 4.2%, and others – 7.2%. After 71 years, the frequency of malignant tumors increases dramatically - mainly BCC and SCC. SGC is less common but occurs in 50% over 71 years Figure 15.

We observed several histological variants of the most common tumor, BCC (Figure 16). The solid (nodular) variant of BCC is the most common (78%), followed by mixed. The rest are in smaller percentages, below 3%.

SURGICAL DESCRIPTIVE ANALYSIS

A total of 429 (95.3%) patients were operated on with local anesthesia and 21 (4.7%) with general or venous anesthesia. Surgical procedures were performed in one stage in 432 (96%) patients and in two or more stages in 18 (4%) patients.

Excision of the tumor was done in two versions: in full and partial thickness of the eyelid. Full-thickness excision for malignant tumors was in 91.3% and in 8.3% for benign tumors. In inflammations, full-thickness excision was not performed (Figure 17). On the other hand, partial-thickness eyelid excision was performed in 75.6% of benign tumors, 17.6% of malignant tumors, and 6.8% of inflammatory tumors ($p<0.001$).

Based on the size, location, and clinical appearance of the tumor, as well as the surgical defect and the adjacent free tissue, various reconstructive surgeries were performed. The distribution is given below in Table 1, and distribution of operative techniques according to the histological variant of the tumor is given in Figure 18.

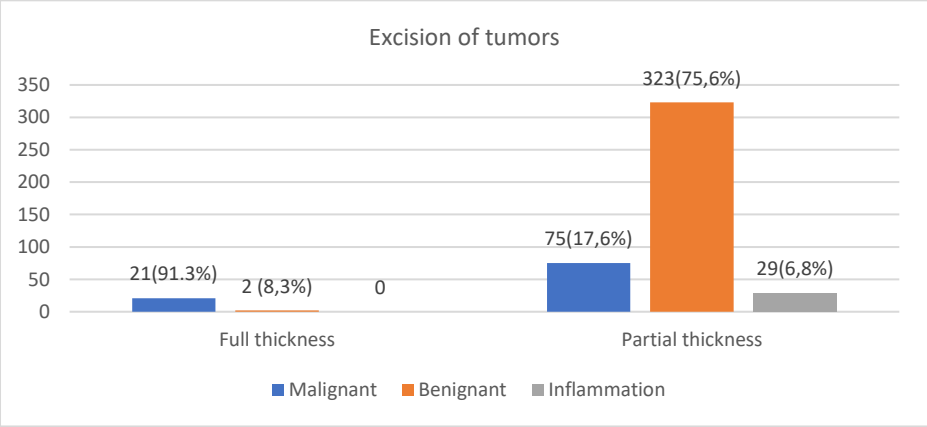


Figure 17. Excision of eyelid tumors versus involvement of eyelid tissues

Direct closure of the operative defect is the preferred method. The type of plastic surgery was chosen according to the clinical judgment of size, location and expected surgical defect. In cases of delayed surgery, the reconstruction is tailored to the histological result.

Table 1. Commonly used operative techniques for closing the surgical defect

Operative technique	Total №	Malignant	Benignant	%
Laissez-Faire	45	3	42	10%
Direct closing	377	69	308	83,8%
Flap technique	14	10	4	3,10%
Glabellar flap	1	1	0	0,20%
Different reconstruction	5	5	0	1,1%
Free skin graft	8	8	0	1,8%
Total	**450**	**96**	**354**	**100,0%**

Significant difference was found when comparing the patients excised in full and partial thickness for the presence of an inflammatory reaction of the surrounding tissues ($p<0.001$). The greatest percentage of partial-thickness excision is in benign tumors without an inflammatory response. The presence of a surrounding inflammatory reaction is positively related to the number of surgical interventions. In the absence of an inflammatory response, 93.5% of the surgeries were performed in one stage and 6.5% in two stages. In the presence of an inflammatory reaction, the percentage of two-stage surgery rises to 16.5%, and one-stage surgery decreases to 83.5%.

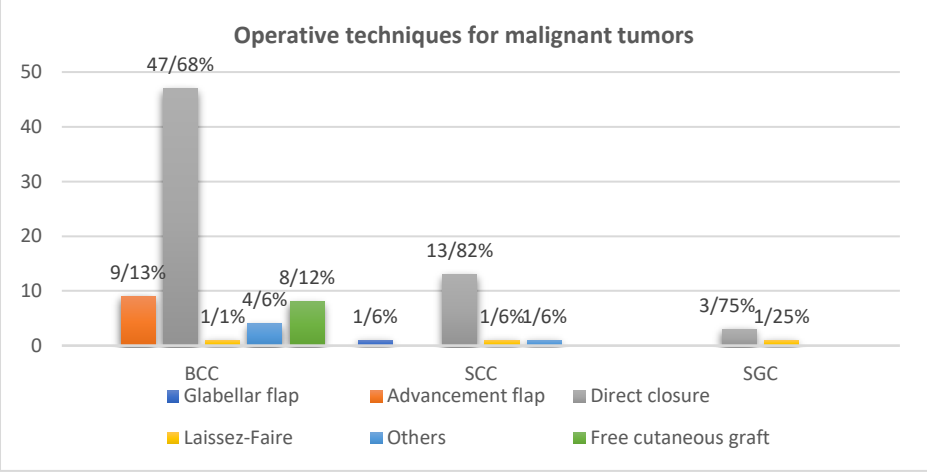


Figure 18. Operative techniques for the three most common malignant tumors.

Out of all 450 surgeries, there were 13 (2.8%) recurrences and 437 (97.2%) without recurrences. Lower eyelid involvement has more recurrences. In the temporal canthal area, 23.1% of recurrences were observed compared to 7.7% in the medial area ($p<0.001$). Recurrences with an involved eyelid margin represent 17.1% of all recurrences, and with an uninvolved margin, they are 1.7%.

Regarding histology, the highest percentage of recurrences is found in BCC -8%, followed by SCC (1%) and SGC (1%) in equal percentages. Of the histological variants of BCC, the highest percentage of recurrence shows the solid variant - 77.4%. The intragroup comparison showed different results – SGC recurred in 25%, BCC – 14.3%, and SCC in 6.25%, making SGC – with the highest recurrence rate.

More recurrences are observed with direct closure 76.9%, followed by advancing flap and free skin graft in equal percentages – 7.7%. One recurrence was observed in benign adipose tissue.

Additional therapy in the form of chemotherapy was given to 2 patients, and radiotherapy – to 3 patients.

ANALYSIS OF DISPERSION

With analysis of variance (ANOVA/ANCOVA) it was determined whether certain factor variables of the categorical type caused systematic variation in a given variable of the quantitative type. For two or more independent variables of categorical type, a multivariate analysis was performed.

The average age of the patients for malignant tumors is 68.86 years; for benign tumors, it is 54.44 years, and for inflammations - 50.55 years. The statistical analysis revealed a significant intergroup correlation of the age indicator for malignant and benign tumors ($p<0.001$) and a non-significant correlation with inflammation ($p>0.273$).

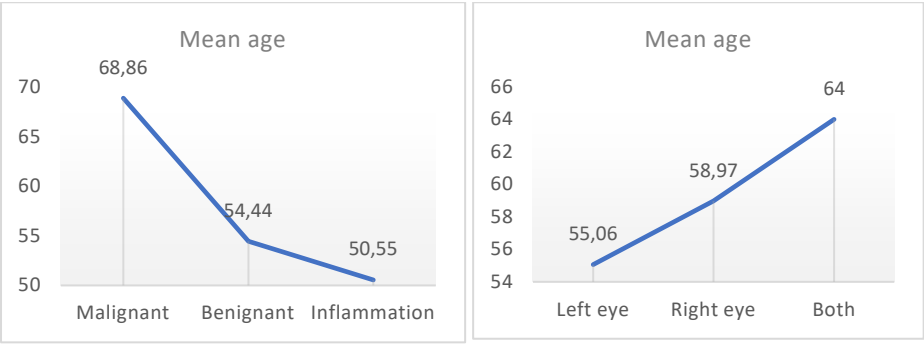


Figure 19. Distribution of mean age by A/malignancy and B/involved eye

The mean age for all with eyelid tumors calculated relative to the affected eye did not show statistical significance despite the borderline p values ($p=0.051$). The mean age for the involved left eye is 55.06 years, for the right 58.97 years, and for bilateral involvement is 64 years. Intragroup-only inflammations showed a significant difference between the two eyes in terms of mean age of involvement – left eye – 34.5 years, and right – 61.8 years. In other words, we can conclude that the inflammations involve the left eye at a younger age than the right, and this is with a significance coefficient of $p<0.001$ (Figure 19).

According to age, we notice a significant difference in favor of engaging both eyelids simultaneously in a later age period ($p<0.007$). The intragroup difference, however, does not exist. The correlation between age and eyelid margin involvement was also significant ($p<0.001$) (Figure 20).

A positive correlation was observed between the indicators of age and recurrence ($p<0.014$), as well as between the duration of the disease and malignancy ($p<0.009$). Relapses are characteristic of a higher average age (Figure 21). Regarding the age of the disease, benign tumors last the longest - 39.3 years, followed by malignant tumors - 21.3 years, and the earliest medical help was sought for inflammation - 12.6 years on average.

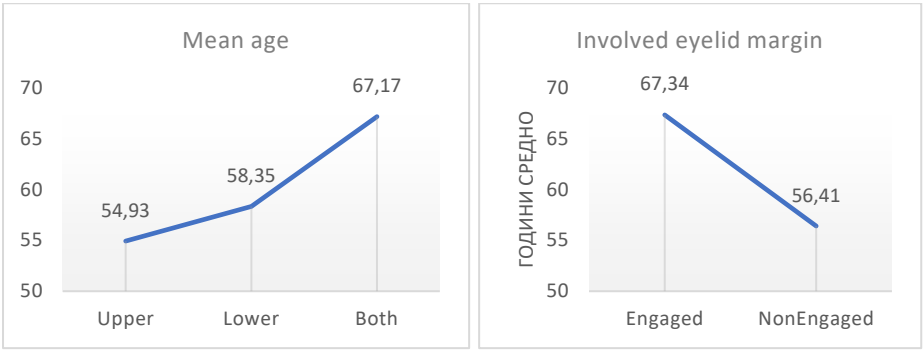


Figure 20. A/Eyelid involvement, B/eyelid margin involvement - by age

Tumor size showed within-group significance for malignant and benign groups and no significance for inflammation. The detailed distribution is given in the descriptive analysis, but from Figure 22, it is evident that the mean size for malignant tumors is 11.68 mm and for benign tumors is 5.71 mm, which has a significance level of p<0.0001.

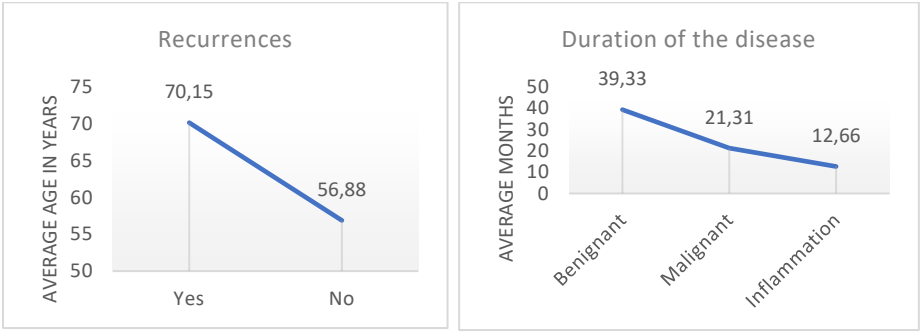


Figure 21. Recurrences / age (p<0.014) (A); Prevalence / malignancy (p<0.009) (B)

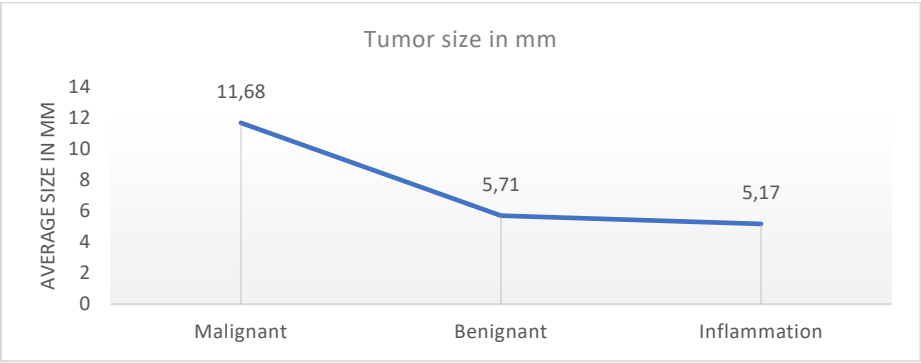


Figure 22. Tumor size ($p<0.0001$)

CORRELATION ANALYSIS

Correlation analysis shows the degree of relationship between the studied indicators. Age and tumor size were not categorical and, therefore, not applicable to analysis such as ANOVA. Bivariate correlation analysis was performed, and Pearson's coefficient (r) was calculated.

There is a positive correlation of age to tumor size with significance ($p<0.01$); also, older age is associated with larger tumor size (Figure 23). The same trend is even more pronounced in malignant tumors as a separate sample.

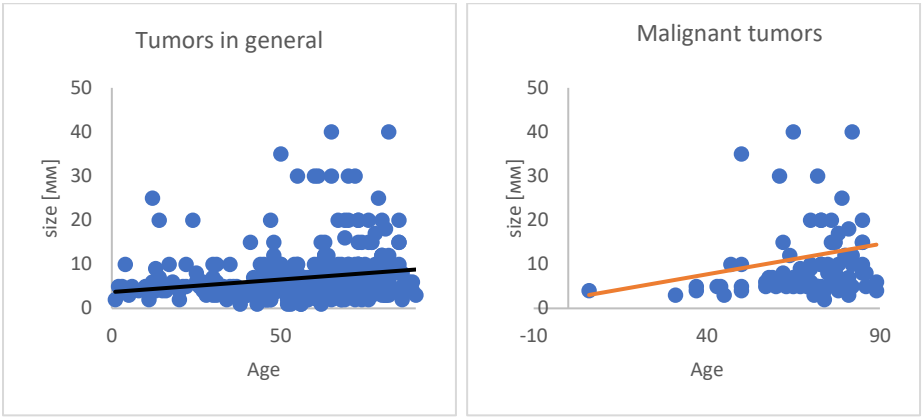


Figure 23. Correlation analysis by age and size ($p<0.01$) - A/ For tumors in general, B/ For malignant tumors

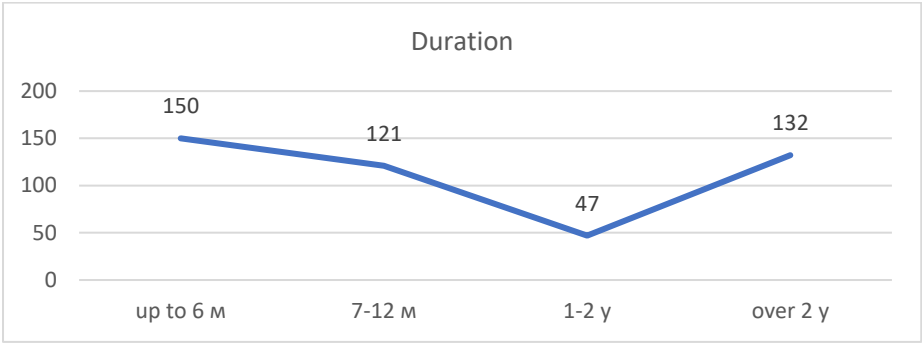


Figure 24. Duration of the disease

Regarding the duration of the disease, there is no significant difference between men and women. A slight decrease is observed in those who sought medical help between the first and second year of the disease (Figure 24).

POSTOPERATIVE RESULTS

After processing the photo documentation of the patients, the anatomical, functional and cosmetic results of the different operative techniques were analyzed.

LAISSEZ-FAIRE

The technique of free healing has been used in patients where the defect is superficial or the tumor is pendiculated, as well as in places where reconstruction is difficult to be done (Figure 25). The wound is not sutured, treated with combined antibiotic/steroid ointments.

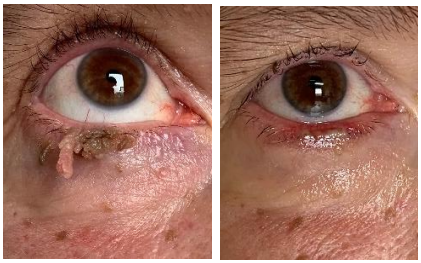


Figure 25. A/B - Patient where the wound was left to heal on its own – laissez-faire.

DIRECT CLOSURE

Direct closure is performed in full and partial thickness. Operative defects where it is certain that the tumor lesion was completely removed are closed directly - 377 (83.8%) cases. An important condition is that there should be no significant traction on the edges of the eyelid wound. Direct closure can be performed with either interrupted or continuous sutures. Most commonly used is 4/0 or 6/0 silk sutures. With a completely excised tumor in a healthy setting, the results are very good (Figure 26).

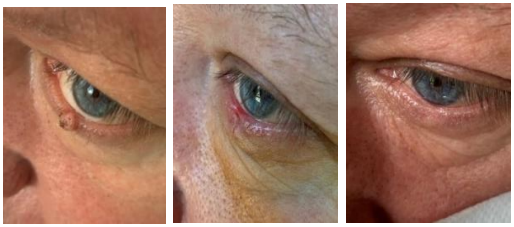


Figure 26. A case of direct closure in partial thickness - A/ before the operation, B/ on the seventh day, C/ on the 30th day

In the case of direct closure of full-thickness eyelid margin defects, sufficient laxity of the eyelid must be present to allow the edges of the wound to be pulled and sutured together without pathological traction. Eyelid laxity was preliminarily examined with the BUTT test. The defect is marked with a surgical skin marker at 3 mm from the tumor and for melanomas - at 9 mm.

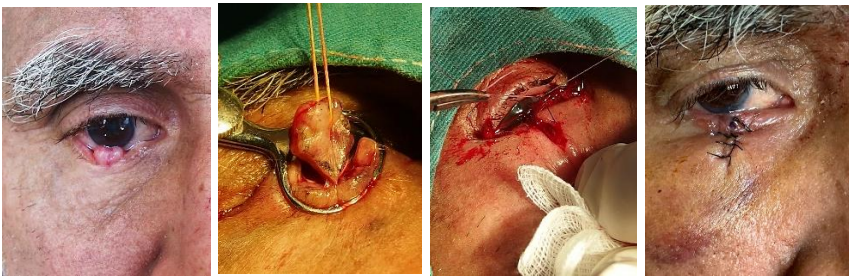


Figure 27. Full-thickness lower eyelid defect - A/before surgery, B- full-thickness excision, C/D-suturing..

Full-thickness direct closure was performed with layer-by-layer adaptation of the posterior first and then of the anterior eyelid lamella. The tarsus is fixed with 6/0 vicryl, and if possible, the knots are left subcutaneously so as not to scratch the cornea. The eyelid margin is adapted with 4/0 - 6/0 silk or nylon, leaving the ends long so that they can be attached to the forehead or cheek to exert traction on the lower eyelid. The goal is good adaptation of the eyelid margin (Figure 27). Depending on the position of the defect and its proximity to the eyelid margin, direct wound closure was performed following the lines of least traction described by Thaler.

ADVANCED AND ROTATION FLAP

Different types of flaps, harvested from adjacent intact skin areas, have been used for excisional defects that do not allow direct closure. Flap with the appearance of geometric figures or letters - rhomboid, round, rectangular or Z, Y, V - shapes, etc., were used. Depending on whether they move or pull, we distinguish advancing, rotation, etc. types of flaps (Figure 28,29).

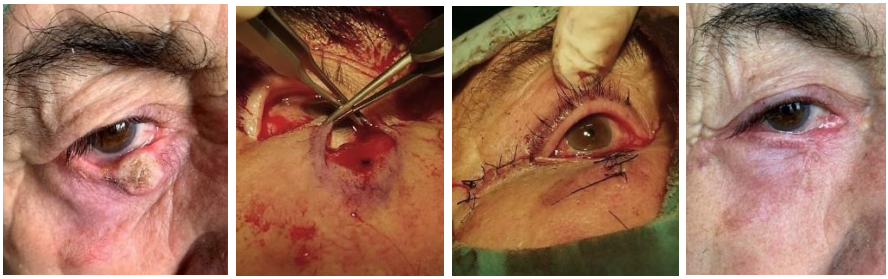


Figure 28. Defect covered with an advancment flap - A/before surgery, - B/trial traction, C/ direct closure with a detachment of the temporal ligament, D/ 30 days

Figure 29. Rotational flap - A/marking the flap, B/rotation, C/closure of the defect, D/ 1 month after surgery

The flap suturing is done in one layer, and mostly 4/0-6/0 silk is used. Its size is increased to compensate for postoperative retraction with subsequent additional traction resulting in a change in eyelid position.

The choice of flap is determined by the location, the size of the operative defect and the availability of suitable adjacent tissue.

GLABELLAR FLAP

We have applied glabellar flap to an excisional defect in the area of the medial canthus of the eyelid. The prepared flap, cleared of underlying tissues, is cut and transposed over the wound defect, always in size exceeding the wound due to expected postoperative retraction.

The forehead wound is closed in layers, with silk, nylon, or prolene 2/0 and vicryl 4/0, or in a single layer with silk or nylon mattress sutures. The flap is fixed to the surgical defect with 4/0-6/0 silk (Figure 30).

Mattress sutures are placed to firmly attach the transposed flap to the wound bed. It increases the flap's chances of survival. In some cases, a silicone or gauze pad is additionally placed to further press the flap to the wound bed.

Figure 30. Glabellar flap in a patient with a large medial canthus defect – A/marking, B/C – preparation and suturing, D/ at 3 months

RECONSTRUCTION CUTLER-BEARD

This technique is applied when there is an operative defect with loss of tissue in the entire thickness and width of more than 1/3 of the eyelid margin of the upper eyelid. It's done in two stages. The first stage is the preparation of a full-thickness advancing flap from the lower eyelid, which passes under a skin bridge separated from the eyelid margin and the tarsus. This bridge is formed after a horizontal incision 4-5 mm below the margin of the lower eyelid, a place corresponding to the end of the tarsus. The advancement flap thus formed is sutured layer by layer to the

excision defect of the upper eyelid. When advancing, the flap pulls on the surrounding tissues, which is why it needs to be relaxed through Burow's angles. The formed bridge of the lower eyelid remains free above the advanced flap.

Figure 31. Plastic surgery of the upper eyelid by the Cutler-Beard method - A/B - skin bridge, C/ 1 month after breaking the bridge

Sutures from the wound are removed on the 7-8th day. In the second stage, after 3-4 weeks, both eyelids are separated 2 mm below the desired position for the upper eyelid. On the thus divided upper eyelid, we removed 2 mm of skin and muscle, and the conjunctiva was inverted and sutured onto the lash line. The lower flap is positioned under the bridge and fixed in layers with interrupted sutures. If possible, the lower eyelid depressor is sutured back to the tarsus (Figure 31)..

RECONSTRUCTION WITH MEDIAL TRANSPOSITION, TARSAL GRAFT, AND PERIOSTEAL STRIP

Medial transposition, tarsal graft, and periosteal strip reconstruction has been used in a large medial defect where marked postoperative medial ectropion is expected (Figure 32,33).

After excision of the tumor, a full-thickness medial defect and a healthy eyelid were formed temporally. The operation begins with detaching the healthy temporal part of an eyelid, together with the adjacent structures (eyelid margin, skin, muscles) from the temporal canthal junction and the

transposition with subsequent suturing of this part to the medial canthal junction, if it is preserved, or to the periosteum in the medial canthal zone.

Figure 32. Medial transposition – A/B – medial surgical defect, C/transposition, D/ tarsal graft

Thus, a new medial eyelid area and a new temporal eyelid defect are formed. The temporal eyelid defect is repaired with a tarsal graft from the upper eyelid - for the posterior lamella and a flap or free skin graft - for the anterior lamella.

Figure 33. Suturing of A/B- band periosteum to the tarsal graft, C/1 day after surgery, D/ 2 months.

FREE SKIN GRAFT

Free skin grafting has been applied to large surgical defects where sufficient adjacent tissue is lacking. It is especially applicable in the nasal canthal area. In these cases, the operative techniques were chosen between glabellar and free skin grafts. Skin was cut from several locations – the inner side of the forearm, pre- and postauricular area, the eyelids, etc. The graft was prepared after subcutaneous layering with lidocaine 1%. The donor bed is significantly undercut to provide free retraction of the wound lip. 4-6/0 silk is used for suturing (Figure 34-36).

Figure 34 A/.Selection of donor skin, B Infiltration of lidocaine subcutaneously; C/ Preparation of donor skin

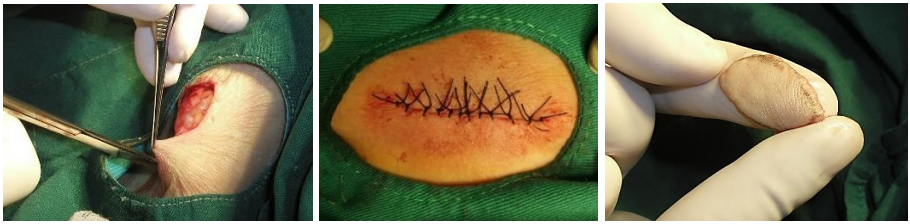


Figure 35.A/ Closure of the donor bed; B/ Postoperative view of the donor bed; C/ Skin graft

After obtaining the donor skin, all subcutaneous tissue is removed and placed in an antibiotic solution until the donor wound is treated. The graft is resized to compensate for shrinkage during wound healing. Mattress sutures are placed to hold the graft to the wound bed (Figure 37).

Figure 36.A/ Removal of subcutaneous adipose tissue from the donor; B/ Positioning the donor on the defect

Figure 37. Case of free skin grafting - A/day 1, B/day 7, C/ 1 year

HUGHES PROCEDURE

Hughes procedure is preferred in cases of a large, full-thickness lower eyelid defect that cannot be closed by any of the methods listed (Figure 38-40).

After the excision of the lower eyelid tumor, sizing and dissecting of the tarsus of the upper eyelid in one with the conjunctiva is carried out. The tarsus prepared in this way is sutured to the lower eyelid at the site of the excision defect, and thus the posterior lamella is restored. A flap from the adjacent tissues or a free skin graft is used for the front lamella. The conjunctival flap is cut at 3rd-4th weeks, depending on the healing process. If ptosis of the upper eyelid is present, the conjunctiva is dissect to the fornix without suturing.

Figure 38. Hughes proceddure-A/tumor, B/operative defect, C/D-reparation of donor tarsus

Фигура 391. Hughes procedure – A/ covering of te wound woth donor tarsus, B/suturing

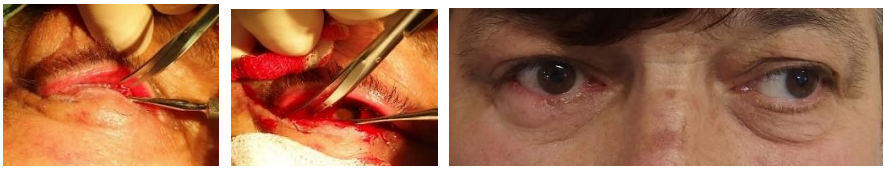


Figure 40. Hughes procedure - A/B - separation of the bridge, C/ 2 months

COMPLICATIONS

The total number of complications for all 450 surgeries was 32 (7%). They were found in the cases with direct closure 20(4%) and plastic 12(3%). Complications are associated with impaired eyelid function, except for those classified as "rough cicatrix with normal function." Relapses are considered separately, and those presented here are the cause of a positional anomaly.

In the case of direct closure, the observed complications are the following: **1. Medial canthus** - ectropion - 5 pcs., dehiscence - 1 pc., rough cicatrix with normal function - 5 pcs., relapse - 1 pc. **2. Temporal canthus** - ectropion -1 pc., relapse -1 pc., **3. Middle eyelid part** - dehiscence - 2 pc., rough cicatrix with normal function - 1 pc., retraction - 2 pc., relapse - 1 pc..

When closing with grfting (including free skin), the observed complications are the following: ectropion - 5 pcs., rough cicatrix with normal function - 3 pcs. , retraction – 1 pc., transplant rejection – 3 pc.

Lower eyelid retraction was observed in a total of 4 patients, which is 12.5% of all complications. The reason is a lack of tissue to cover the operative defect, as a result of which scarring develops (Figure 41). In cases where only the anterior lamella is missing and, the defect is reconstructed with a flap or other skin graft, the graft results in vertical traction. Ectropion is present (Figure 42). It was observed in 11 cases, representing 34% of all complications.

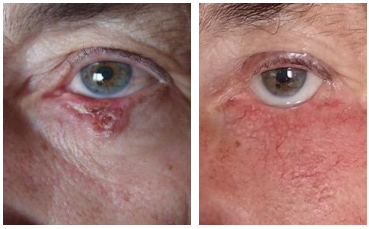


Figure 41. Eyelid retraction due to lack of tissue - A/preoperative, B/postoperative

Figure 42. A/B Postoperative ectropion; Figure 43. Recurrences -A/nodular, B/causing cicatrization

The observed recurrences causing a positional abnormality were 3, which is 9% of all complications. All of them were diagnosed with basal cell carcinoma (Figure 43). Gross cicatrix was observed in 9 cases, which was 28% of all complications (Figure 44).

Figure 44. Rough cicatrix in the first months - A/at 1m, B/at 2m and C/at 9m

Figure 45. Damage to the graft after irradiation/A/, necrosis /B,C/

Graft rejection occurred in 3 patients, which was 9% of all complications. Graft damage was observed in one patient after radiotherapy without leading to complete failure, and in another hemorrhage under the graft (Figure 45) All complications were treated surgically, with the goal of reoperation being functional outcome rather than cosmetic.

DISCUSSION

EPIDEMIOLOGICAL CHARACTERISTICS

The obtained results are based on patients of Ophthalmology Clinic - Pleven for ten years period. The data are not part of an epidemiological study but are entirely clinical.

Table 2 Comparison by epidemiological indicators

Author, Country, Year	Time period	№ of pati-ents	Benign %	Mean Age B	Malignant %	Mean Age M
Asia						
Huang, Taiwan, 2015	1995–2015	4521	95.0	55.4	5,00	72.5
Chang CH, Taiwan, 2003	1994–1998	144	87.5	*	12,50	61
Toshida H, Japan, 2012	1993–2007	118	89.8	47.8	10,20	53.1
Sihota, India 1996	1982–1992	313	43.1	*	56,80	*
Rathod A, India, 2015	2007–2009	100	61.0	37.02	39,00	58.59

Ni Z, China, 1996	1953–1992	3510	68.7	*	31,20	*
Western countries						
Deprez, Switzerland, 2009	1989–2007	4981	82.0	*	18,00	*
Paul S, USA, 2011	2004–2007	855	75.9	<60	24,10	>60
Mclean, AFIP, USA, 1994	1984–1989	846	54.0	*	46,00	*
Font, USA, 2006	1980–1982	1474	60.0	*	40,00	*
Middle East						
Bagheri, Tehran, Iran, 2013	2000–2010	182	45.1	46.4	54,90	63.9
Gundogan FC, Turkey, 2015	2008–2012	1541	92.4	50.08	1,50	68.6
Bulgaria						
Botev, 2006	2002-2005	237	82.1	*	17,90	*
Vasileva, 2006	2004-2006	98	81.6	*	18,40	*
Kapurdov, 2008	2001-2006	370	57.8	*	42,2	*
Madzharova, 2008	2000-2007	132	66.7	48.5	33,30	57
Balabanov, 2010	1990-2009	427	45.67	46	38,90	61
Balchev, 2022	2010-2019	450	71.8	54.4	21,30	68.9

Table 2 shows a comparison between our study and similar cohorts of patients by other authors.

CHARACTERISTICS BY SEX

Of the 450 operated patients, it was found that with a small statistical difference, women predominated 57% (255) compared to men 43% (195). According to the type of tumor (benign, malignant), similar results were observed in both sexes (p=0.97). According to this indicator, we find a similar tendency of distribution among other authors as well.

The gender distribution is even, except for the over-70 group, where there are almost twice as many women as men. From the NSI sample, it is clear that after the age of 70, women are almost twice as many as men. Most

women in the indicated group corresponded to most tumors in them in the same group without being significant.

CHARACTERISTICS BY AGE

The total number of tumors begins to increase after the age of 40. Up to the age of 40, all tumors are 17%, and after that - 83%, but the biggest peak is observed after the age of 60. Tumors after 60 years of age account for 53% of all tumors.

Benign tumors begin to increase in number after age 40 until around age 70, when the increase becomes fourfold, then decreases again. In malignant tumors, we observe a plateau up to 60 years, after which a fourfold and fivefold increase. Our calculation shows that 80% of malignant tumors are after 60 years of age. Benign tumors are characteristic of a younger age, and the gap between the two groups is 20 years. Inflammations show a relatively equal distribution in all age groups. The results are similar to other authors.

From the results, it became clear that the mean age for the involved left or right eye was significant only for inflammations - the left eye was affected at a younger age ($p<0.001$). The reason is not clear and similar data from other authors were not found.

Involvement of both eyelids simultaneously was observed at an older age of 67.1 years and was statistically significant ($p<0.007$). The indicator correlates with late seeking of medical care and does not correlate with gender. The eyelid margin was also involved at an older age of 67.3 years ($p<0.001$). The three factors of eyelid margin involvement: malignancy, tumor size, and age over 60 years were in a positive significant relationship. Recurrences are characteristic of a higher average age ($p<0.014$). The main factor for this is incomplete surgical excision, the location and depth of tumor invasion, postponement of tumor surgery. We found a positive correlation of age to tumor size ($p<0.01$), older age was associated with larger tumor size and larger size with malignancy.

CHARACTERISTICS BY RESIDENCE

The characteristic by place of residence, compared with the statistics provided by NSI at the beginning of 2021, shows that 72% of tumors are in a city, and 28% in a village. Cross-sectional analysis showed that the older population (60+ years) with eyelid tumors mostly lived in villages ($p<0.002$). Malignant cases in villages represent 31.5% ($p<0.001$), and in cities – 17.2%. Benign ones show the opposite ratio – 68.5% in villages and 82.8% in cities. Our discussion, as well as that of other authors, confirms the fact that people living in a city have easy and quick access to medical services.

CHARACTERISTICS BY TYPE AND LOCATION OF THE TUMOR

Most tumors are benign - 323 (71.8%), followed by malignant - 96 (21.3%), inflammation - 29 (6.5%) and the least are precancers - 2 (0.4%). A number of authors show similar results; on the other hand, there are authors who show twice the percentage for inflammation than we do. The difference is whether hordeolums fall into the sample. This defines our result as average rather than an exception.

Of the malignant tumors, the largest share is BCC, followed by SCC. In terms of degree of malignancy, MM ranks first, followed by SGC. Over 60 years of age, a threefold increase in malignant tumors is seen, and over 70 – a sixfold increase. The percentage of benign tumors is 7-8 times greater than that of malignant tumors, but upon reaching 71+ years, the ratio levels off significantly and represents - 53% to 48%. Tumors in women were more than those in men in both malignant and benign groups, as was observed in the total amount of tumors and with similar rates of distance. A comparison between our study and other authors' studies is presented in Table 2.

Of the total number of tumors, the upper eyelid is involved in 44.8% of cases, the lower - in 50%, and both eyelids - in less than 2%. Malignant

tumors more often involve the lower eyelid. - 67.7%, compared to the above 21.9%, and in 10.4% both eyelids are involved. The percentage ratio of the three parts of the eyelid was not found in other authors. Benign tumors are relatively evenly distributed between the lower and upper eyelids, but with a preponderance toward the upper eyelid in 50% to 45%. Data for other authors compared with our study are presented in Table 3.

The medial canthal area is involved in 65.4% of all tumors compared to 34.6% for the temporal area. Of all tumors affecting the medial canthal area, 64% were malignant and 36% benign, and 63% malignant, 37% benign in the temporal canthal area ($p>0.37$). This establishes the medial canthus as the preferred location, compared to the temporal, for all tumors, not just malignant ones. Separately for malignant tumors, the medial canthus was involved in a ratio of 80% to 20% relative to the temporal ($p<0.029$).

Table 3 Distribution of eyelid tumors by author and year

Country	Author	Year	Upper eyelid %	Lower eyelid %	Medial canthus %	Lateral canthus %
Localization of all malignant tumors						
Bulgaria	Mihailova	2008	5	53	21	12
Bulgaria	Madzharova	2008	15,9	68,2	9,1	6,8
Bulgaria	Nenkova	2010	10,1	72,9	13,2	3,8
Bulgaria	Zlatarova	2010	4,8	85,7	4,8	4,8
Bulgaria	Balabanov	2010	26,5	40,8	22,4	10,2
Bulgaria	Balchev	2022	44,9	50,0	3,0	1,1
Romania	Coroi	2010	43,7	47,1	7,2	1,9
Pakistan	Hussain	2013	25,7	32,9	8,1	0,9
USA	Tierney	2013	16	44	19	4
Localization of BCC						
Bulgaria	Chilova	2006	X	59,1	24,8	x
Bulgaria	Sredkova	2008	8.3	50	20,8	8.3

This determines the advantage of the operative techniques related to the reconstruction of defects in the region of the medial canthus and of defects of the lower eyelid. The temporal location of the tumors gives us more opportunities to reconstruct the operative defect, due to the presence of adjacent free skin, while in the case of a medial defect, reconstruction with adjacent tissues is highly limited due to the anatomical configuration of the area. Excision itself at the medial approach is challenging because it is difficult to assess the depth of tumor infiltration, and it quite often invades inward to the orbit.

Histological control of the margins of the excised tissue is important to the procedure. Reconstruction is started after establishing clean histological edges and bottom of the wound. In the area of the medial canthus it is difficult to achieve such, therefore it is appropriate to do the reconstruction in two stages, to be able to wait for the histology, which will show whether a new excision is necessary.

We found that the involvement of the eyelid margin in malignant tumors is 83%, and in benign tumors - 17%. This is due to the invasive ability of malignant tumors. Eyelid margin involvement by age, for the 61-70 years and 71+ years groups, accounted for 20% and 60% of all cases with involvement ($p<0.001$).

We analyzed the cases where we have involvement of the eyelid margin in combination with involvement of the eyelid skin near the eyelid margin (25.7%), as well as in combination with involvement of the medial canthus (14.3%) ($p<0.001$) . We can conclude that involvement of the eyelid margin is a characteristic of malignant tumors, and skin involvement near an already involved eyelid margin and medial canthus increases the probability of malignant histology by 49%. The presence of an inflammatory reaction of the surrounding tissues is relevant to the surgical judgment. However, it was found that the inflammatory reaction in malignant tumors represents 48.1%, in benign (cyst, papilloma) - 34.2%, and in some inflammatory tumors (mycosis, etc.) it is 7.7% ($p<0.001$). The inflammatory reaction in malignant tumors can be associated with the occurring necrosis, and in benign tumors with mechanical irritation of the tumor protruding above the skin.

A significant relationship was found between size and malignancy. Small sizes are characteristic of benign tumors and inflammations, while large sizes are characteristic of malignant tumors ($p<0.001$). Sizes below 10 mm - the statistical distribution is in favor of benign tumors (50-80%); above 10 mm - malignant tumors prevail (> 50%). Small tumors up to 10 mm represented the majority of the sample (89%), and those larger than 10 mm accounted for 11%. Small tumors are easily removed and mostly closed directly, while large tumors require reconstruction.

The most common malignant tumor of the eyelids is BCC and accounts for 71.9% of malignant tumors. According to a number of authors, the large percentage of BCC at an older age is characteristic of the Caucasian race, but it is the opposite for the Asian race: the largest percentage of malignant tumors falls on SCC, and in second place is BCC. All of our patients were defined as Caucasian.

We compared our tumor percentage distribution data with that of the Mayo Clinic, provided in the following diagram (Figure 46).

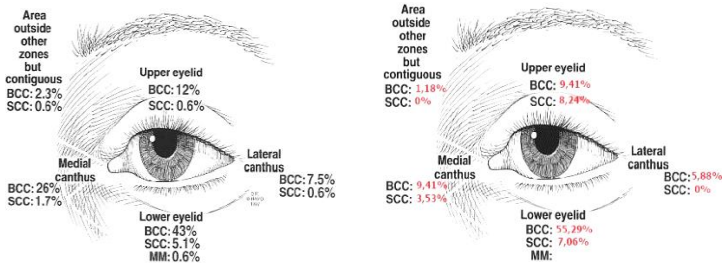


Figure 46. A) Mayo Foundation, B) Pleven Ophthalmology Clinic

In our patients, in contrast to the data reported by the Mayo Clinic, BCC occupies a larger proportion and is not equally distributed but significantly more represented on the lower eyelid. SCC showed a higher percentage ratio and was distributed evenly between the upper and lower eyelids.

SURGICAL TREATMENT

All patients were operated under a microscope. The reconstruction of the surgical defect follows the principle of a good anatomical, functional and, if possible, cosmetic result.

ANESTHESIA

The most sparing anesthesia for eyelid tumors is local. Lidocaine (1-2%) pure or in combination with Marcaine 1/3 and Adrenalin (1:100,000) was mainly administered. The maximum safe dose of 2% lidocaine solution is 15 ml (4mg/kg). Low-concentration epinephrine is administered to reduce bleeding. Marcaine prolongs the effect of local anesthesia. In the presence of adrenaline, the safe dose of lidocaine 2% is 20 ml; for 1% lidocaine – the doses are doubled. In some patients, local anesthesia was administered concurrently with intravenous Fentanyl premedication. In 21 patients with a major surgical intervention or at the patient's request, general anesthesia was preferred.

When identification of the levator and depressor muscles is required, it is appropriate to administer intravenous anesthesia with the patient well anesthetized but conscious and able to perform basic commands. Such anesthesia was preferred in two patients with upper eyelid reconstruction. Medium-dose intravenous propofol was administered. Inhalation anesthesia is also possible for short-term procedures.

TUMOR EXCISION

The first stage in eyelid tumor surgeries is excision. At this stage, it is important to achieve tumor-free lines after excision in healthy skin and to form a wound defect suitable for reconstruction.

Excision can be partial thickness for a lesion involving the anterior lamella, or full thickness, involving both lamellae. Of all full-thickness

excisions - 91.3% were performed for malignancy, which is directly related to the low recurrence rate.

Marking the tumor defect in helthy skin is an important stage in the pre-operative evaluation. If the clinical judgment is in the direction of a malignant tumor, the marking is wider - "in healthy" (3-4 mm) for BCC and SCC, and MM - 8 mm and more.

For topographical-anatomical orientation, the histological material should be marked, which is done with different colored surgical sutures. This provides information on where there is incomplete excision and re-resection is needed. There are several histological variants of the most common eyelid tumor (BCC) such as Morphea or advancing BCC, which are known to be locally advanced (laBCC) or metastatic (mBCC). During surgery we can only assume that we cut into "a helthy skin". In case of doubt, the wound is not closed but left open for a week after thorough coagulation and antibiotic ointment. After the histology comes out, we revise the wound. We are now aware if the excision lines are tumor-free or if they are not - where we need to re-excise according to the marking. MOHS surgery is not applicable in our clinic.

For eyelid tumors, the generally accepted TNM classification, which determines the approach and treatment for tumors in other parts of the body, is not particularly applicable. References to this classification could only be made in cases of melanoma malignum (MM) insofar as it could be related to MM with a cutaneous localization. The Clark and Breslow classifications alone or in combination are advantageous in staging melanoma of the eyelids, but in general, they are also not fully relatable to the eyelids.

The choice of operative procedure depends mainly on the location of the tumor, the size and shape of the surgical defect. Generally, tumors larger than 10 mm require reconstruction, regardless of their histology. The aim is primarily to restore the anatomical function of the eyelids, regardless of the cosmetic result, which can be corrected at a later stage.

SPONTANEOUS GRANULATION „Laissez-faire”

According to the literature, ⅓ of the entire thickness of the lower eyelid can be missing and left to spontaneous granulation; however we have left much smaller lesions and mostly superficial ones. After 6-8 weeks, the wounds heal with an acceptable cosmetic result. This, of course carries the risks of an uncontrolled cicatrix that will lead to a positional anomaly. In our study, no complications were observed with the Laisez-faire technique.

DIRECT CLOSURE OF THE OPERATIVE DEFECT

Direct closure of front lamella. The excision should be sized to allow direct closure with horizontal traction of the eyelid skin. We have achieved this by undermining the edges of the wound defect, which provides mobilization of the skin. We have avoided vertical traction, as it causes positional anomalies of the eyelid, and in case of impossibility, we have reconstructed with plastics extending the traction line. Their purpose is, by displacing the flap along the course of the operative defect, to provide a relative lengthening of the traction line, which will lead to less pull and hence to less positional anomaly.

In direct closure of an eyelid wound, skin suturing can be performed with an interrupted or continuous suture of various types of suture materials. Nylon and prolene sutures are monofilament, leaving a smaller postoperative cicatrix than silk sutures. They do not cause a local inflammatory reaction, but healing is slower. Silk thread stimulates inflammation around the suture, leading to rapid wound healing, but is associated with greater postoperative cicatrix. With the silk thread, we removed the stitches at 7-8 days, and with the nylon and prolene at 8-10 days.

Full-thickness direct closure follows the same principles as horizontal closure of a vertical wound defect. For direct full-thickness closure to be possible, it is necessary to have sufficient laxity of the remaining parts of the eyelid after the excision. The two halves of the eyelid should be able

to touch each other with moderate traction. To provide another 1-2 mm length of the eyelid margin, we cut the temporal canthal ligament of the affected eyelid. The medial canthal ligament should be preserved if possible, but in some cases, we cut it as well.

Another condition for good direct closure of full-thickness defects is a correct, perpendicular to the eyelid margin incision on both sides of the tumor, which after the tarsus, we have extended downwards in a spear-like fashion to a pentagon shape. This enables a good ajustment of the wound and avoids a "dog ear" deformity. In an upper eyelid defect, our incision is again perpendicular to the lash line but triangular, not lanceolate, as in the lower eyelid, due to the crescent shape of the upper tarsus.

The wound is closed in two layers. First, we sew the two halves of the tarsal plate to each other with 2-3 stitches. 6/0 vicryl as the knots are left intra-palpebrally. Then we fix the eyelash margin with one or two silk threads - 6/0, passing along the "grey line". If one rather than two sutures are used on the eyelid margin, a U-shaped suture is preferred. This gives us better stabilization. The sutures stabilizing the lash line are often left long to attach to the forehead (for the lower eyelid) or to the cheek (for the upper eyelid), which will provide additional traction to the wound defect.

For direct closure of defects in the area of the medial canthus and nose, we use vertical stabilizing sutures. They provide additional stabilization of the wound and follow the course of the natural curvature of the corresponding part of the face.

Skin sutures are usually removed every 7-10 days. In cases with pronounced cicatrization, the earlier removal of the sutures is required, but this carries the risk of wound dehiscence. A few of our patients required the addition of an adapting suture at the eyelid margin due to wound dehiscence after a dropped primary suture.

RECONSTRUCTION

CLOSURE WITH A FLAP

Closure with a flap is applied when the operative defect is large and direct closure is impossible. It is important that there is enough adjacent tissue from which a flap can be formed. We have used an advancing, transpositional, or rotational flap - alone or as part of a combined plastic.

The options are: skin flap or skin-muscle flap. We have preferred the skin flap in cases of covering a skin defect. In the absence of part of the underlying muscle, we prefer a skin-muscle flap. If the muscle layer is not involved, detachment of the skin-muscle flap will cause rough postoperative cicatrix. Then additional stabilization of the injured region or a change in the direction of traction by transposing a muscle is necessary.

When the skin flap is very taut, retraction occurs, leading to necrosis of the distal margins and part of the flap falling off. The skin-muscle flap is rare because the skin-muscle flap brings blood vessels to the bed of the wound defect. It never necrotizes the entire flap because the flap contains donor vasculature at its base.

When tailoring the flap, it is always oversized because in the process of healing the surgical wound, the flap contracts and causes traction. This process is strictly individual and depends on the structure of the surrounding tissue, but in our cases, we have resized the flap so that it is 2-3 mm larger than the operative defect. To reduce the traction of the flap, we have undermined its base or the place of rotation much more than necessary.

An essential point in the survival of the flap is a good adaptation. Good adaptation is a function of three key surgical moments. The first moment is to handle the points of pull or rotation. In case of rotation, advancement, or transposition of the place of rotation, there is an infolding of the skin with subsequent thickening, called "dog ear". It causes deformation and additional traction. In advancing flap, these areas are relaxed by cutting Burow's triangular flap, rotational flap with an

additional skin incision, and transpositional flap - with additional undermining. The second point determining a good adaptation is the ratio of the thickness of the flap to the thickness of the skin in the recipient bed. To obtain a uniform postoperative cicatrix, we have equalized these two thicknesses. Excessive thinning is also not preferable as there is a risk of flap contraction. The third point determining a good adaptation is the adhesion of the flap to the recipient bed. Tight adherence is associated with the development of good vascularization in the wound. In our patients, this was accomplished by mattress sutures across the flap and a compression bandage or bolster. Mattress sutures are placed in areas of anatomical curves where the graft does not adhere well to the recipient bed. Poor contact of the flap with the recipient bed leads to the accumulation of fluid and blood under the flap and its subsequent compromise, while good contact contributes to rapid vascularization.

We sutured the flap mainly with silk because it can cause a local inflammatory reaction around the thread, which in this case, is desired. If the flap is skin-muscular, it is possible to suture in two layers with vicryl and silk.

On the first postoperative day, all flaps appear pale. Flaps that have an underlying hematoma, dropped sutures, wound dehiscence, etc., look different. After 1-2 days, the color from white gradually turns pink, which is a sign of good flap survival. In our study, we observed several cases in which the flap necrotized partially - along the peripheral margin. Our approach to these cases, was determined by the extent of necrosis. In cases with a small area of necrosis, the wound was allowed to heal using the Laissez-Faire method. When a large part of the flap falls off - we choose a free skin graft or replace it with a new flap, where the adjacent tissues allowes. Putting lubricants on the flap also contributes to its survivability. We used antibiotic ointments.

FREE SKIN GRAFT

A free skin graft is used for defects that cannot be closed directly or with a flap. We have used skin from the preauricular, postauricular, brachium

area, or other eyelids. The upper eyelid and preauricular region are closest in texture to the skin of the eyelids, and the lack of hair follicles makes them the first choice donor site; however, for larger defects, skin from the brachium has been used. The presence of a graft with a hair follicle on the eyelid area changes the aesthetic outcome in patients.

When taking a skin graft, it is oversized again because the skin graft contracts to 1/3 when healing. The donor bed must be closed directly; therefore, the donor skin is taken in the shape of a "leaf". We have injected lidocaine 1% subcutaneously, which simultaneously anesthetizes and exfoliates the skin that will be taken as a graft. The resulting graft was placed in a solution containing an antibiotic until the donor wound was treated. The closure of the donor bed is done after wide undermining of the surrounding skin so that there is no additional traction. In cases where we chose the preauricular region as a donor, the undercut was made just between the skin and subcutaneous fat to avoid contact with the facial nerve. Suturing of the donor bed is performed with interrupted silk or nylon sutures. We have more often sutured the preauricular bed in two layers with the goal of a smaller postoperative facial cicatrix. The subcutaneous tissue is sutured with Vicryl 4-6/0 and the skin with intradermal Prolene 5-6/0, aiming for a smaller cicatrix.

Adaptation of the donor to the recipient bed is important for its survival. Excess subcutaneous fat, muscle tissue and part of the dermis were removed. When tailoring the donor to the surgical wound, an average of 2-3 mm is relaxed on each side, depending on the size of the defect. It is sutured with interrupted silk sutures 6/0 silk. An important point in the survival of the graft, and in this operation, is the placement of full-thickness mattress sutures that press the graft to the bed, as well as a bolster or compression dressing. The bigger the defect, the more mattress sutures are placed.

In cases of poor adjustment or small graft size, it is possible to necrotize part of the graft. Necrosis occurs at the edges of the wound, where the nutrition of the new tissue is poor. In these cases, we replaced the graft or, if the defect was small, we allowed it to primary granulate. Graft survival was judged by its color change by the 3rd postoperative day. As

with flap reconstruction, the free skin graft is white on the first operative day because of the absence of blood vessels and changes color to pink after revascularization begins. In the first postoperative months, the graft appears raised and different in color from the surrounding tissues due to its greater thickness. Around the sixth month, its texture becomes similar to the surrounding tissue, and its color lightens. For a good adaptation of the graft in the bed, it is important that it is larger than the size of the wound, that it is pressed with enough mattress sutures, and that the bed is well coagulated to avoid hemorrhage under the graft that would lead to necrosis.

In our study, we had 1 case of a serious complication with hemorrhage under the graft unrelated to the operative intervention. In this case, the transplant was replaced. We have also had one case of mild ectropion due to a small graft resulting from a poor fit. No correction was necessary.

COMBINED TECHNIQUES

BRIDGE FLAP (CUTLER-BEARD)

We have applied this operational procedure when there is an operative defect with a loss of tissue in full thickness or width of more than 1/3 of the eyelid margin of the upper eyelid and when it is impossible to apply another reconstruction. Possible operations for such a defect are: transposition of the donor tarsus, Swift flap (reverse Hughes), etc., as in the specific case, we have chosen a bridge flap.

Particular care is needed in aligning the excision defect of the upper eyelid so that its edges are part of a rectangle to ensure a good congruence to the transposed flap. The flap must be well prepared and mobile so that it can be easily transposed to the upper eyelid. It is fixed in layers with multiple interrupted stitches. During the reconstruction, we make sure that the bridge remains vital and free, as we have regularly treated it with ointment. We proceed to divide the eyelids after the flap is completely healed to the upper eyelid, which occurs around the 4th week. A good cosmetic and functional result depends on the correct treatment of the

bridge with subsequent readaptation to the lower eyelid. The main concerns are bridge necrosis, which we did not observe in our cases. After the secondary reconstruction of the lower eyelid, the bridge healed well. Our surgical outcome is similar to the literature data. Auricular cartilage can be placed in the place of the missing tarsus, or part of the preserved tarsus can be transposed - we did not replace a missing tarsus in this case.

As a complication, we can report a few dropped sutures, which were restored with new ones. The operation restores the anatomy and a large part of the function of the eyelid, but the aesthetic result is not very good.

HUGHES PLASTIC

The Hughes procedure has been used in the reconstruction of large full-thickness defects of the lower eyelid where direct closure was not possible, even after disruption of the temporal canthal ligament. When treating the lower eyelid wound, it is important to get the lateral wound edges strictly perpendicular to the eyelid margin so that we can properly suture the donoric tarsus to the remnants of the lower eyelid tarsus. Observance of the rectangular shape of the defect is also decisive for the detachment of an advancing flap from the lower eyelid, which covers the transposed tarsus and forms the anterior lamella. In cases where it was not possible to cover the defect with an advancing flap, we used a free skin graft from the periauricular or brachial areas.

When taking a donor tarsus from the upper eyelid, we followed several important topographical-anatomical rules. The distal tarsal incision starts 4 mm from the eyelid margin, not to affect the hair follicles or cause a positional abnormality of the upper eyelid. If the defect of the lower eyelid is 100% of its length, the donor tarsus that we would get from the upper eyelid will have a rhomboid shape, and after suturing it to the edges of the defect, we will not get an even eyelid margin. Therefore, we find it a better option to take 80% of the length of the tarsus to obtain a rectangular shape and to cover the difference of 20% of the defect with a break of the lower temporal canthal ligament or, if this is not enough, with exfoliation on a periosteal band from the temporal orbital margin.

Conjunctival dissection along with the donor tarsus was always done to the superior fornix to ensure a stable blood supply, little traction, and coverage of the donor bed.

The conjunctival bridge is left in all operations for two weeks, but a longer period is also possible. In the second week, it is cut with scissors, and the strip of donor conjunctiva is sewn to the newly formed eyelid margin. To prevent ptosis of the upper eyelid, we prepare the conjunctiva overlying the donor bed back to the superior fornix.

This technique gives very good anatomical, functional and cosmetic results. The disadvantage is the length of the operative procedure.

GLABELLAR FLAP

The glabellar flap performed in the studied period are few in number, but those traced from another period are more. This gives us a reason to analyze the technique. Operative defects in the area of the medial canthal area are difficult to reconstruct due to the presence of a particular anatomical architectonics, different texture and thickness of the skin in this area. Tumors in this area primarily involve the skin but often penetrate deeply, possibly into the orbit. This requires a deeper and wider excision, which in turn makes the reconstruction more complicated. The possibilities for reconstructions in this area are free skin graft, glabellar plastic, or a combination of both. Transposition of a flap from the adjacent upper or lower eyelid to the medial canthal area always ends with an unsatisfactory cosmetic and compromised functional result due to difficult adaptation of the flap, gross cicatrix, or edge necrosis. Glabellar flap is a modified V-Y rotation flap that is taken from the area between the two eyebrows, called the glabella. The technique is not difficult, but the problem comes from the different skin of the glabella and eyelids. On the one hand, it is necessary to preserve the vascularization of the glabellar flap, and on the other hand, the flap itself is thick and needs to be thinned, which compromises vascularization. We have undermined the skin flap completely, especially at the base of the nose, so that it can be freely transposed. However, at the base of the nose,

we operate subcutaneously because of the underlying nerves. To obtain a good functional and anatomical result, we must increase the size of the tailored glabellar flap by about 2-3 mm, and to obtain a good cosmetic result, we must reduce its thickness at the point of attachment to the upper eyelid skin.

In case of a very large defect, we do not always succeed in reconstructing with only glabellar flap and then we cover the rest of the wound with free skin graft.

The edges of the glabellar wound are undermined so that there is no pulling and a rough cicatrix - it is sutured in two layers. When suturing the wound, the eyebrows converge and the face acquires a somewhat sad look, which is well tolerated in adult patients.

The placement of mattress sutures and/or bolster ensures a good fit and follows the anatomical curves of the medial area. These mattress sutures are directly related to flap survival. If it does not adhere well, fluid collects under the flap, which peels it off and causes it to be rejected.

With this operative technique, a disadvantage can be necrosis of a part of the flap or positional anomalies of the eyelid. In one of the cases, we observed such partial necrosis of the flap. The necrotic area is removed, and the wound is allowed to heal secondary. The final result of this complication is also satisfactory, but as a drawback, we consider the different pigmentation in the area of necrosis compared to the surrounding area, which becomes barely noticeable over time.

In the early postoperative period, the glabellar flap is rough and thick, but with time, it thins and acquires a similar structure to the rest of the skin, which provides a satisfactory cosmetic result. This is an individual process, but for the majority of patients, it occurs around the sixth month.

MEDIAL TRANSPOSITION

Medial transposition, in combination with a tarsal graft and a periosteum band, is not widely described in the literature and is a relatively new method in oculoplastic surgery, especially in eyelid tumor surgery.

In our study period, this technique was applied to one patient with a tumor that covered the medial 2/3 of the lower eyelid, including the eyelid margin and lacrimal punctum. There are more observed patients from other periods. With such a formed medial defect, we have several options for reconstruction, among which - free skin graft in combination with a tarsal or cartilage graft, reconstruction according to Hughes, etc., including medial transposition. The disadvantage of all of them is the lack of a proper eyelid margin, and especially of the eyelashes themselves. This leads to an unsatisfactory cosmetic result even with a good functional and anatomical one. In medial transposition, the absence of eyelashes is repositioned temporally. From a cosmetic point of view, the absence of eyelashes and an irregular eyelid margin are more tolerated if they are temporary.

An important point for the survival of the graft and the transposed portion of the eyelid is the application of mattress sutures with/without a bolster. They press the transposed structures into each other and facilitate the emerging blood supply.

The method gives very good cosmetic and functional results, but drastically increases the operative time. It also requires a well-trained surgical team.

EARLY POSTOPERATIVE PERIOD

We consider the time from the operation to the seventh day for the early postoperative period. In most cases, the wound is closed with a bandage until the 3rd day, after which we leave it open to "breathe", which contributes to its faster healing. On day 7-8, all skin sutures are removed. In the early postoperative period, it is observed mainly for signs of

infection. In case of wound dehiscence, which can happen when the sutures are cut or poor primary adaptation of the graft/lamb to the wound bed, we refresh the wound edges and replace the dropped sutures.

In the first few days, we observe the survival of the transplant or flap, which we judge by its color; as mentioned, it goes from pale to pink until after a few months, it acquires its original color. It turns black with necrosis. In our study, we observed several partial rejections in free skin grafting and one case of sub-graft hematoma that resulted in necrosis of the entire graft. Our approach to graft necrosis is described next to each operation. In plastics, especially glabellar, in the early postoperative period, the cosmetic result is poor, and surgeons with little experience may worry.

We have not observed infections in the early postoperative period.

LATE POSTOPERATIVE PERIOD

The late postoperative period begins on the 7th day after suture removal. Complete healing is individual; in most cases, it is around the sixth month. In operations for tumors, our attention is mainly directed to the presence of recurrences and not only to the healing period.

In the course of its healing, the surgical wound passes through the phases of reparative inflammation. In the first month, a young connective tissue with a red cicatrix is observed, and in some patients – a more pronounced proliferation with the formation of an uneven wide cicatrix. The next phase of wound healing is associated with the transformation of fibrous tissue into mature connective tissue that has the ability to contract. The contraction leads to the formation of irregular cicatrixes, pulling the surrounding tissues, which in turn leads to a violation of the position of the eyelids. Despite the successful surgery, the healing process is individual and in some patients it is more pronounced to the extent of keloid.

Positional anomalies are a major complication after eyelid tumor surgery. Ectropion, entropion and trichiasis are mainly observed. Mild positional abnormalities may be present, but with a good functional outcome. In this case, additional surgical intervention can be avoided. In cases where we have a good anatomical and functional result but a bad cosmetic one (pigmentation, cicatrix), an additional cosmetic procedure can be started after the sixth month, when we think that the recovery period of the wound has ended.

We observe for recurrences on the 3rd and 6th month after the operation. In cases with local metastasis in BCC and SCC, re-excision is performed in a healthy area with histological control of the edges without waiting for complete healing of the wound. The moment of detection of local recurrences is an indication of a new operation.

Patients with malignant eyelid tumors are sent to an oncocommission.

RADIATION AND CHEMOTHERAPY

In ophthalmology, the approach is different from that of other clinical disciplines and often does not coincide with them.

According to the literature, radiation therapy for eyelid tumors is rarely applied, mostly postoperatively, and requires very careful planning. We mainly rely on histological control after excision. In deep tissue involvement or tumor involvement of the orbit, and in cases where radical excision cannot be performed, we might refer the patient for radiotherapy, but this is rare. In the setting of a well-done reconstruction or transplant, radiation therapy will compromise the healing process. In our study, we observed a patient irradiated postoperatively who rejected the transplanted skin structures; we observed dehiscence of the surgical wound, relaxation of the flap, and damage to the surrounding healthy tissues. In the case of preoperative radiotherapy, we observed atrophy of the adjacent skin, which becomes parchment-thin, making it unsuitable for reconstruction. Contraction and atrophy in the eyelid area cause cicatrixes and positional anomalies that compromise both the

physiological and cosmetic outcome; therefore, we have avoided the preoperative application of radiotherapy. However, if a decision is made for radiotherapy, direct consultation with a radiologist is appropriate to assess the radiosensitivity of the tumor and the size of the irradiated area.

Proton treatment is more suitable for ophthalmology than X-rays. The disadvantage is the cost of the treatment, as well as its lack in our country.

The side effects of radiotherapy are many - the lens and cornea are directly damaged by X-rays, despite the precautions taken, which leads to a decrease in vision.

Destructive radiotherapy (chemical or thermal burning) as a treatment method for eyelid tumors is also not a good alternative to surgery, due to the lack of histological control of the treated area.

Chemotherapy for eyelid surgery is divided into local and systemic. The general disadvantage of medical treatment is the lack of histological control of the primary tumor. The assessment is clinical, based on the appearance of the tumor and the impression of regression or progression.

Of the possible drugs for local chemotherapy, we used only Mitomycin-C in a patient with an eyelid tumor involving adjacent tissues as an adjunct to the rest of the therapy.

In systemic chemotherapy, we have very good impressions of vismodegib in BCC alone and in combination with surgical excision. Postoperative chemotherapy reduces the recurrence rate. In our patient, after the excision of the primary tumor, small areas of involvement remained, the excision of which would cause difficult-to-reconstruct defects. Systemic chemotherapy with vismodegib had an extremely good effect – the areas involved by the tumor shrank and disappeared. The two methods of treatment, surgery and chemotherapy, are potentiated, and the results are very good.

Drug treatment is rarely used on its own. It is usually combined with other types of treatment. Due to its high value in many countries, including Bulgaria, the protocol for its application requires surgical treatment to be carried out first and, in case of failure, to include medication. Drug

treatment has several side effects, as it also attacks healthy cells; therefore an adequate benefit-risk assessment of the therapy needs to be made.

CONCLUSIONS

1. Correlational dependences were established between indicators of malignancy, tumor size, eyelash margin involvement, gender, age, etc..
2. The incidence of eyelid tumors is similar to other authors, but varies according to the histological result.
3. We confirm the world statistics, according to which BCC is the most common tumor of the eyelids. The generally accepted TNM classification for tumors is not applicable to eyelid tumors.
4. Treatment of eyelid tumors is mainly surgical. The success of the surgery depends on:
    a. Radical excision of the tumor.
    b. The choice of an appropriate reconstructive technique.
    c. A special approach to the most difficult areas to reconstruct: the medial canthus and the lower eyelid.
    d. Small details of surgical technique, such as mattress sutures, graft tailoring and thinning, are directly related to graft survival.
5. Correct preoperative planning and selection of the surgical intervention ensures the anatomical, functional and cosmetic result of the surgery.

CONTRIBUTIONS

1. **Contributions of an original nature**
    a. A detailed clinical and statistical analysis of tumor diseases of the eyelids and treatment methods was carried out according to data from the Ophthalmology Clinic Pleven.
    b. A descriptive analysis is made in 2019; however for the first time a dispersion and correlation analyses of eyelid tumors to patients of Ophthalmology Clinic Pleven for a period of ten years (2010-2019) is made.
    c. The histological variability of eyelid tumors for the considered period is analyzed and compared with other periods.
    d. For the first time in Bulgaria, a medial transposition with a tarsal graft and a periosteum strip is applied to cover medial lower eyelid defects.
    e. Introduction of Vismodegib drug treatment for eyelid BCC for the first time.
2. **Contributions of an affirmative nature**
    a. The incidence of tumor diseases was compared with the literature data.
    b. The criteria for the selection of the operative technique were compared.
    c. The criteria for radiation and chemotherapy were compared.
3. **Contributions of a scientifically applied nature**
    a. An analysis was made of the operative approach in the different groups of reconstructive procedures
    b. An assessment of the functional, anatomical and cosmetic outcome in surgery of eyelid tumors was made, as well as the possibility of its optimization.
    c. An assessment of postoperative wound healing was made.
    d. The combined application of glabellar and free skin grafts in one operation for very large defects was introduced.
    e. An assessment of the applicability of the TNM classification in ophthalmology was made

PUBLICATIONS AND SCIENTIFIC ANNOUNCEMENTS RELATED TO THE DISSERTATION

Publications

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2. *G. Balchev, Ch. Balabanov, S. Murgova.* Neurofibromatosis – diagnostic challenges. Български Офталмологичен Преглед, 2020; 1 (64), 46-49 doi: http://dx.doi.org/10.14748/bro.v64i1.6670
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Scientific announcements

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