

Indications for eye removal over a 13-year period at an ophthalmology referral center in São Paulo, Brazil

Indicações para remoção ocular ao longo de um período de 13 anos no centro de referência oftalmológica em São Paulo, Brazil

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ABSTRACT

Purpose: To analyze the indications and types of eye removal at Latin America's highest-volume ophthalmic reference center in São Paulo, Brazil.

Methods: A retrospective analysis was conducted of surgical pathological reports in the electronic database of the Ophthalmology Department of the Universidade Federal de São Paulo Hospital of patients who underwent eye-removal procedures between January 2000 and December 2012.

Results: A total of 412 cases met the inclusion criteria for this study. The most common indications for eye removal were ocular melanoma and retinoblastoma, representing 35.4% and 31.1% of the total cases, respectively. Other frequent indications included endophthalmitis (6.3%), nonspecific inflammation (4.1%), squamous cell carcinoma (3.6%), panophthalmitis (3.4%), and phthisis bulbi (1.2%). The remaining indications accounted for 14.8% of all cases, with each accounting for <1% of the total cases. Enucleation was the most common eye-removal procedure seen in our study.

Conclusions: The two most common indications for eye removal were ocular melanoma and retinoblastoma. Alternative treatment options are effective in limiting the need for eye removal but are constrained by our public center's socio-economic context.

Keywords: Eye enucleation; Eye evisceration; Retinoblastoma; Melanoma; Brazil

RESUMO

Objetivo: Analisar os tipos e indicações para a remoção dos olhos no maior centro de referência oftalmológica da América Latina em São Paulo, Brasil.

Métodos: Revisão retrospectiva de laudos cirúrgico patológico em uma base de dados eletrônica do Departamento de Oftalmologia do Hospital da Universidade Federal de São Paulo. Foram analisados pacientes submetidos ao procedimento de remoção oftálmica no período de janeiro de 2000 a dezembro de 2012.

Resultados: Um total de 412 casos estiveram de acordo com os critérios de inclusão desse estudo. A indicação mais comum para remoção oftálmica foi Melanoma ocular e Retinoblastoma, representando, respectivamente, 35,4% e 31,1% do total de casos. Outras indicações frequentes incluíam Endoftalmite 6,3%, Inflamação inespecífica 4,1%, Carcinoma escamocelular 3,6%, Panoftalmite 3,4% e Phthisis Bulbi 1,2%. O restante das indicações totalizaram 14,8% de todos os casos, sendo que cada um correspondem com menos de 1% do total. Enucleação foi o procedimento de remoção oftálmica mais comum observado em nosso estudo.

Conclusão: As duas indicações mais frequentes para remoção oftálmica no centro oftalmológico de referência do Brasil foi melanoma e retinoblastoma. Opções terapêuticas alternativas são efetivas para limitar a necessidade da remoção ocular, porém são restritos devido ao contexto socioeconômico de nossa população.

Descritores: Enucleação ocular; Evisceração do olho; Retinoblastoma; Melanoma; Brasil

INTRODUCTION

The removal of a diseased eye is an aggressive intervention performed as a last resort, often for the treatment of infections refractory to medical management, malignant tumors, or blind painful eyes. Recommendation for eye removal can be very difficult for both patients and ophthalmologists.

Evisceration is the surgical removal of the eye's contents, with the exception of the sclera and extraocular muscles. It is indicated in the treatment of resistant endophthalmitis and in blind painful eyes after the possibility of a malignant tumor has been excluded. Enucleation involves complete removal of the globe from the orbit, leaving the other orbital structures intact. When a malignant intraocular tumor is suspected and other treatment modalities are not available or indicated, enucleation is often the intervention of choice. Exenteration involves complete removal of all orbital contents. This procedure is generally reserved for treating eyes with orbital disease, including ocular tumors⁽¹⁻⁴⁾.

Multiple studies demonstrate that surgical indications for eye removal vary widely, depending on the availability of alternative treatment modalities such as radiotherapy, referral practices, and the prevalence of the disease in question⁽⁵⁻¹⁰⁾. In developing countries, access to funding and expertise can also affect treatment.

Few studies have addressed the issue of the frequency and indications of eye removal in Brazil. Here we present Latin America's largest and longest retrospective analysis to review the indications and types of eye removal performed.

METHODS

All surgical pathological reports during the period from January 1, 2000, to December 31, 2012, in the database of the Ophthalmology Department at the Universidade Federal de São Paulo's (UNIFESP) Hospital were reviewed that contained at least one of the following keywords: eye, orbit, eyelid, ocular, or conjunctiva. Patients' charts

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were reviewed to determine the patient's age and sex, the anatomical structure from which the specimen was taken, the surgical procedure performed to obtain the specimen, the pathologist's diagnosis, and whether an evisceration, enucleation, or exenteration was performed. If all data points were available, the de-identified patient information was included in the study.

RESULTS

Over this 13-year study period, 3446 unique patient ophthalmological specimens were received at the Pathology Department coming from the Ophthalmology Department of the UNIFESP Hospital, of which 412 specimens were associated with eye-removal procedures. This represents 12% of the total number of surgical ophthalmological specimens.

The number of eye-removal procedures varied each year. From 2000 through 2012, the total number of eye-removal procedures per year fluctuated from eight to 81 (Figure 1). The most common indications for eye removal as well as the number of each procedure type for each indication are featured in table 1. The seven indications listed in table 1 accounted for 85.2% of the total eye-removal procedures performed across the 13-year study period. The indications in the remaining 61 eyes (14.8%) consisted of various other pathologies. Seven pathologies were associated with between two and five eyes (Table 3), and 42 pathologies were associated with only one eye (Table 4).

Of the 412 patients who underwent eye-removal procedures, 234 (56.8%) were male and 175 (42.5%) were female. Three patients (0.7%) with retinoblastoma had absent information regarding sex. The patients' age ranged between 4 months and 102 years, with a mean of 34.8 years. Table 2 provides an overview of patients' age and sex for the seven most common indications for eye removal in the study sample.

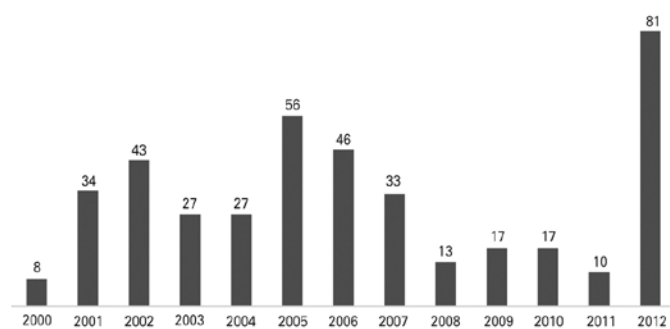


Figure 1. Total number of eye-removal procedures per year from 2000 to 2012 inclusively.

Table 1. Frequent indications for eye removal

Diagnosis	N° of cases	Evisceration	Enucleation	Exenteration
Melanoma	146	0	135	11
Retinoblastoma	128	0	128	0
Endophthalmitis	26	11	15	0
Nonspecific inflammation	17	12	5	0
Squamous cell carcinoma	15	0	12	3
Panophthalmitis (acute)	14	0	14	0
Phthisis bulbi	5	5	0	0

DISCUSSION

Eye removal is an aggressive procedure generally reserved for eyes with malignant tumors, eyes with certain advanced diseases, blind painful eyes that are not well controlled by medication or neurolytic agents, and trauma cases. Indications range from ocular cancer to preventable causes such as trauma or neglected diabetes, where secondary glaucoma may result in a blind painful eye. In some regions, such as Brazil, indications for eye removal may be related to access to health care.

We found ocular melanoma to be the most common indication for eye removal at our center. We observed a nonlinear trend in the total number of eye-removal procedures performed annually at our center over the 13-year study period.

Small-sized and medium-sized melanomas may be treated by plaque radiotherapy, whereas enucleation is frequently performed for large tumors, as well as for small-sized and medium-sized tumors when plaque radiotherapy is unavailable. Because of federal regulations and other factors, plaque radiotherapy is not available to all patients in the public healthcare system in Brazil. Although our center does offer plaque radiotherapy to patients in the public healthcare system, plaques have not been available at our center since 2010 because of funding reallocations. Thus, enucleation is the primary treatment approach for ocular melanoma when plaque radiotherapy is unavailable. This may account for the spike in eye-removal procedures seen from 2011 ($n=10$) to 2012 ($n=81$).

Unfortunately, we did not have access to follow-up data to determine how many enucleations resulted following plaque radiotherapy before 2012. This reality has prompted our group to conduct a prospective study treating choroidal melanomas with primary vitrectomy and endoresection. The details of this study are pending publication.

Retinoblastoma was the second most frequent indication for eye removal in our study. Advanced retinoblastoma can be cured in most cases by enucleating the eye, but less advanced cases can be treated with systemic chemotherapy and local modalities such as laser photocoagulation or cryotherapy. Unfortunately, in Brazil, retinoblastoma

Table 2. Age and sex information

Diagnosis	Age range (years)	Mean age (years)	Sex		
			Male	Female	unknown
Melanoma	19-93	51.5	81	65	0
Retinoblastoma	0.33-27	2.7	84	61	3
Endophthalmitis	27-102	59.5	13	13	0
Nonspecific inflammation	5-82	41.1	9	8	0
Squamous cell carcinoma	35-84	51.5	12	3	0
Panophthalmitis (acute)	15-83	53.7	11	3	0
Phthisis bulbi	1-79	21.2	3	2	0

Table 3. Frequency of less common indications for eye removal

Diagnosis	Frequency
Nonspecified carcinoma	5
Coats' disease	4
Basal cell carcinoma	2
Keratoses	2
Blood clot (embolic, thrombotic)	2
Medulloepitheliomas	2
Melanocytoma	2

Table 4. Single patient diagnoses

Actinic keratosis	Malformation of the anterior chamber	Organized hemorrhage of origin probably from pyogenic granuloma
Acute keratitis	Malignancy	Organized subretinal bleeding (hemorrhage). Fibrovascular subretinal membrane
Acute uveitis	Malignancy of blue cells	Recent hemorrhage
Adenoid cystic carcinoma	Malignancy undifferentiated with extraocular extensions	Retinal atrophy, retinchoroiditis scars, fibrosis with neovascularization, vitreous hemorrhage
Choroid hemangioma	Medulloepitheliomas teratoid	Sebaceous carcinoma
Chronic cerato-scleritis	Medulloepitheliomas teratoid ciliary body	Sebaceous glands carcinoma
Chronic iridocyclitis	Melanocytoma ciliary body	Shred of ocular conjunctiva with large hemorrhagic areas
Chronic keratitis	Metastasized carcinoma committing choroid, ciliary body, and iris	Traumatic perforation of the ocular globe
Ciliary body adenocarcinoma	Metastasized hepatocellular carcinoma	Trichoblastic carcinoma
Circumscribed choroidal hemangioma. Subretinal hemorrhage. Atrophic retina and optic nerve	Metatypical carcinoma	Undetermined histogenesis neoplasia
Corneal drilling with disruption of ocular structures and choroid	Microfocus calcification at cribriform level	Undetermined histogenesis neoplasia with large areas of necrosis and hemorrhage
Diffuse uveoscleritis not granulomatous	Mucoepidermoid carcinoma	Without residual neoplasia
Glaucoma	Neoplasms 100% necrotic	Xanthogranuloma juvenile
Keratitis interstitial	Ocular globe malformation	

is often diagnosed when the disease is in an advanced stage, and therefore a large percentage of patients are treated by enucleation⁽¹¹⁾. In a study by Leal-Leal et al., 500 cases of retinoblastoma from 16 centers in Mexico were retrospectively analyzed according to various pathological and demographic criteria⁽¹²⁾. The authors reported that 84.9% patients were treated by enucleation and concluded that the development of an early detection program and treatment protocol for retinoblastoma was necessary at the national level in Mexico. Although our study did not address enucleation rates in patients with retinoblastoma, previous studies have highlighted that retinoblastoma is generally diagnosed at later stages in developing countries^(13,14), leading to increased enucleation rates and decreased survival rates⁽¹⁵⁾.

In 2012, our center introduced intra-arterial chemotherapy as an effective alternative to enucleation for advanced cases of retinoblastoma⁽¹⁶⁾. These cases are not reflected in the number of enucleation procedures reported in this study. Given the use of this new modality, we anticipate a significant reduction in the number of enucleations of eyes with advanced retinoblastoma and thus a significant reduction in the total number of eye-removal procedures at our center.

Ocular melanoma and retinoblastoma were the most common indications for eye removal at our center over the 13-year study period. A Serbian study reviewed 586 cases of patients who underwent enucleation and similarly found that the most common indication was melanoma, followed by retinoblastoma⁽¹⁷⁾. Although our study addressed all forms of eye removal, enucleation was the most common procedure performed, and it was the most common procedure used to treat both melanoma and retinoblastoma.

Our results differ from the most recent Brazilian analysis of eye removals at the Araujo Jorge Hospital, a single center 1000 km northwest of São Paulo, by Sirianni et al.⁽¹⁸⁾ This was a retrospective review of 269 cases of malignancy in the ocular cavity and indications for eye removal. The authors reported that basal cell carcinoma was the most common malignancy seen, representing 58% of the total cases. In our sample, basal cell carcinoma accounted for two cases (0.5%; not listed in the results because of the low frequency). In the study of Sirianni et al., melanoma accounted for only 6.7% cases, in contrast to 35.4% cases in our study. These differences are most likely accounted for by increased ultraviolet exposure to the north of São Paulo and delay in referral in this relatively underserved region.

Like our study, the study of Sirianni et al. reported that enucleation was the most common surgical procedure used to treat retinoblastoma and ocular melanoma, whereas exenteration was used in most cases of squamous cell carcinoma of the conjunctiva and all cases of basal cell carcinoma. The Araujo Jorge Hospital and our facility are not designated trauma centers, which accounts for the absence of trauma as an indication for eye removal in both data sets.

Another study reviewed the clinical causes for ocular enucleation in 1375 cases from a single center in Beijing, China⁽¹⁹⁾. The study found that enucleated eyes accounted for 29.5% of all cases sent to the pathology department, which is significantly higher than the 12% we report for all eye-removal procedures at our center. In that study, trauma accounted for 62.5% of all enucleation procedures, followed by tumors at 28.5%. In our sample, trauma accounted for two cases (0.5%; not listed in the results because of the low frequency). Collectively, these differences highlight the importance of evaluating the indications for eye removal in a regional-specific and center-specific manner.

As shown in tables 1 and 3, other indications for eye removal were frequently observed in our study. Evisceration or enucleation was the procedure used to treat all cases for the listed indications, with the exception of invasive squamous cell carcinoma, in which three cases (20% of all squamous cell carcinomas) were treated by exenteration. Endophthalmitis accounted for 6.3% of all indications for eye removal. A previous report found that older age, absence of light perception, endophthalmitis associated with corneal ulcer, and endogenous endophthalmitis were risk factors that were significantly associated with endophthalmitis leading to enucleation or evisceration⁽²⁰⁾. Unfortunately, we were not able to compare patients with endophthalmitis who underwent eye removal with those who did not.

Contrary to the sum of existing literature, ocular melanoma and retinoblastoma accounted for most eye-removal procedures during our 13-year study period. This difference is most likely because of referral patterns in the São Paulo area that limit the number of trauma cases seen in our center, the difficulty in accessing nonsurgical oncological treatment for some of our patients, and the often delayed presentation of patients to the clinic.

Orbital and ocular tumors are best treated at an early stage. The recent introduction of intra-arterial chemotherapy for retinoblastoma at our center, as well as efforts to treat choroidal melanomas with

primary vitrectomy and endoresection, may significantly decrease the total number of eye-removal procedures at our center in the coming years, although eye removal will still account for a substantial proportion of surgical procedures.

The rate of enucleation for tumors is high in our series, in contrast to declining trends reported from other parts of the world. The morbidity associated with the procedure can have a significant impact on the patient's self-esteem, workplace productivity, and quality of life, especially when vision loss is unnecessary.

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