Prognostication of uveal melanoma is simple and highly predictive using the cancer genome atlas (TCGA) classification: A review.

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ABSTRACT

PURPOSE:

The cancer genome atlas (TCGA) is a comprehensive project supported by the National Cancer Institute (NCI) in the United States to explore molecular alterations in cancer, including uveal melanoma (UM). This led to TCGA classification for UM. In this report, we review the American Joint Committee on Cancer (AJCC) classification and TCGA classification for UM from the NCI's Center forCancer Genomics (NCI CCG) (based on enucleation specimens [n = 80 eyes]) and from Wills Eye Hospital (WEH) (based on fine needle aspiration biopsy [FNAB] specimens [n = 658 eyes]). We then compare accuracy and predictability of AJCC versus (vs.) TCGA.

METHODS:

Review of published reports on AJCC and TCGA classification for UM was performed. Outcomes based on AJCC 7th and 8th editions were assessed. For TCGA, UM was classified based on chromosomes 3 and 8 findings including disomy 3 (D3), monosomy 3 (M3), disomy 8 (D8), 8q gain (8qG), or 8q gain multiple (8qGm) and combined into four classes including Class A (D3/D8), Class B (D3/8qG), Class C (M3/8qG), and Class D (M3/8qGm). Outcomes of metastasis and death were explored and a comparison (AJCC vs. TCGA) was performed.

RESULTS:

In the NCI CCG study, there were 80 eyes with UM sampled by enucleation (n = 77), resection (n = 2), or orbitotomy (n = 1) and analysis revealed four distinct genetic classes. Metastasis and death outcomes were subsequently evaluated per class in the WEH study. The WEH study reviewed 658 eyes with UM, sampled by FNAB, and found Class A (n = 342, 52%), B (n = 91, 14%), C (n = 118, 18%), and D (n = 107, 16%). Comparison by increasing class (A vs. B vs. C vs. D) revealed older mean patient age (P < 0.001), worse entering visual acuity (P < 0.001), greater distance from the optic disc (P < 0.001), larger tumor diameter (P < 0.001), and greater tumor thickness (P < 0.001). Regarding outcomes, more advanced TCGA class demonstrated increased 5-year risk for metastasis (4% vs. 20% vs. 33% vs. 63%,P < 0.001) with corresponding increasing hazard ratio (HR) (1.0 vs. 4.1, 10.1, 30.0,P= 0.01 for B vs. A andP < 0.001 for C vs. A and D vs. A) as well as increased 5-year estimated

risk for death (1% vs. 0% vs. 9% vs. 23%,P < 0.001) with corresponding increasing HR (1 vs. NA vs. 3.1 vs. 13.7,P= 0.11 for C vs. A andP < 0.001 for D vs. A). Comparison of AJCC to TCGA classification revealed TCGA was superior in prediction of metastasis and death from UM.

CONCLUSION:

TCGA classification for UM is simple, accurate, and highly predictive of melanoma-related metastasis and death, more so than the AJCC classification.

Conservative management of retinoblastoma: challenging orthodoxy without compromising the state of metastatic grace. "alive, with good vision and no comorbidity"

Munier FL, Beck-Popovic M, Chantada GL, Cobrinik D, Kivelä TT, Lohmann D, Maeder P, Moll AC, Carcaboso AM, Moulin A, Schaiquevich P, Bergin C, Dyson PJ, Houghton S, Puccinelli F, Vial Y, Gaillard MC, Stathopoulos C

ABSTRACT

Retinoblastoma is lethal by metastasis if left untreated, so the primary goal of therapy is to preserve life, with ocular survival, visual preservation and quality of life as secondary aims. Historically, enucleation was the first successful therapeutic approach to decrease mortality, followed over 100 years ago by the first eye salvage attempts with radiotherapy. This led to the empiric delineation of a window for conservative management subject to a "state of metastatic grace" never to be violated. Over the last two decades,conservative management of retinoblastoma witnessed an impressive acceleration of improvements, culminating in two major paradigm shifts in therapeutic strategy. Firstly, the introduction of systemic chemotherapy and focal treatments in the late 1990s enabled radiotherapy to be progressively abandoned. Around 10 years later, the advent of chemotherapy in situ, with the capitalization of new routes of targeted drug delivery, namely intra-arterial, intravitreal and now intracameral injections, allowed significant increase in eye preservation rate, definitive eradication of radiotherapy and reduction of systemic chemotherapy. Here we intend to review the relevant knowledge susceptible to improve the conservative management of retinoblastoma in compliance with the "state of metastatic grace", with particular attention to (i) reviewing how new imaging modalities impact the frontiers of conservativemanagement, (ii) dissecting retinoblastoma genesis, growth patterns, and intraocular routes of tumor propagation, (iii) assessing major therapeutic changes and trends, (iv) proposing a classification of relapsing retinoblastoma, (v) examining treatable/preventable disease-related or treatment-induced complications, and (vi) appraising new therapeutic targets and concepts, as well as liquid biopsy potentiality.

Ophthalmic vascular events after intra-arterial chemotherapy for retinoblastoma: real-world comparison between primary and secondary treatments.

Ancona-Lezama D, Dalvin LA, Lucio-Alvarez JA, Jabbour P, Shields CL.

ABSTRACT

PURPOSE:

To determine whether treatment order affects ophthalmic vascular event rates after intra-arterial chemotherapy (IAC) for retinoblastoma.

METHODS:

Patients who received IAC as primary or secondary treatment for retinoblastoma from January 2009 to January 2018 were included. All eyes were imaged with fundus photography and fluorescein angiography. Patient characteristics and vascular event rates were compared using t-test and Fisher's exact test.

RESULTS:

There were 196 patients treated with 682 infusions of IAC, divided into primary (no previous therapy, 98 eyes of 98 patients, 328 infusions) and secondary (after other therapy, 105 eyes of 98 patients, 354 infusions) treatment. Overall, ophthalmic vascular events were found after 5% of infusions (17% eyes). A comparison of ophthalmic vascular events (primary vs. secondaryIAC), with mean three infusions per eye (median 3, range 1-7), revealed no difference in overall percentage of eyes affected (18% vs. 15%, P = 0.57). Adverse vascular events per eye included retinal vasculature attenuation (1% vs. 0%, P = 0.99), peripheral retinal pruning (1% vs. 0%, P = 0.99), branch retinal artery occlusion (0% vs. 1%, P = 0.99), central retinal artery occlusion (0% vs. 1%, P = 0.99), macular ischemia (0% vs. 2%, P = 0.51), vitreous hemorrhage (2% vs. 3%, P = 0.92), subretinal hemorrhage (1% vs. 0%, P = 0.99), retinal pigment epithelium atrophy (6% vs. 3% P = 0.43), choroidal atrophy (4% vs. 2%, P = 0.92), optic disk pallor (1% vs. 0%, P = 0.99), and ophthalmic artery occlusion (9% vs. 6%, P = 0.35).

CONCLUSION:

Ophthalmic vascular events after IAC for retinoblastoma affect only 5% of eyes per infusion (17% of treated eyes). Vascular event risk per eye is similar when using IAC as primary or secondary treatment.

Intravitreal anti-vascular endothelial growth factor for the management of neovascularization in retinoblastoma after intravenous and/or intraarterial Chemotherapy: long-term outcomes in a series of 35 eyes.

Stathopoulos C, Gaillard MC, Moulin A, Puccinelli F, Beck-Popovic M, Munier FL.

ABSTRACT

PURPOSE:

To report the use of anti-vascular endothelial growth factor in the management of retinoblastoma.

METHODS:

Retrospective review of 35 eyes (33 patients) treated with at least one intravitreal anti-vascular endothelial growth factor (ranibizumab and/or aflibercept) for new iris (n = 26) and/or retinal neovascularization (n =21) after intravenous chemotherapy and/or intraarterial chemotherapy.

RESULTS:

Most eyes (n = 31/35, 89%) were Group D or E. Previous treatments were salvage intraarterial chemotherapy after intravenous chemotherapy (n = 21/35, 60%), first-line intraarterial chemotherapy (n = 7/35, 20%), and first-line intravenous chemotherapy (n = 7/35, 20%). Associated clinical features were retinal ischemia (94%), retinal detachment (51%), active tumor (34%), intravitreal hemorrhage (43%), and/or glaucoma (17%). Mean 1.6 anti-vascular endothelial growth factor injections/eye were given; 28 eyes received ranibizumab, 2 aflibercept, and 5 both agents. Eight eyes underwent complementary treatments of ischemic retina. Resolution of neovascularization was observed in 28 eyes (n = 28/35, 80%). Globe salvage was achieved in 51% (n = 18/35), including 25% of those with active tumor (n = 3/12). One eye became phthisic. Sixteen eyes were enucleated, nine for tumor relapse/progression. Five eyes had high-risk histopathologic risk factors and received adjuvant intravenous chemotherapy. All patients are alive with no extraocular extension nor metastases (mean follow-up 3.7 years, range 1.1-7.6).

CONCLUSIONS:

Intravitreal anti-vascular endothelial growth factor contributed to a globe salvage rate of 51% by providing conditions to continue conservative treatment.

Optical coherence tomography biomarkers to distinguish diabetic macular edema from pseudophakic cystoid macular edema using machine learning algorithms.

Hecht I, Bar A, Rokach L, Noy Achiron R, Munk MR, Huf W, Burgansky-Eliash Z, Achiron A.

ABSTRACT

PURPOSE:

In diabetic patients presenting with macular edema (ME) shortly after cataract surgery, identifying the underlying pathology can be challenging and influence management. Our aim was to develop a simple clinical classifier able to confirm a diabetic etiology using few spectral domain optical coherence tomography parameters.

METHODS:

We analyzed spectral domain optical coherence tomography data of 153 patients with either pseudophakic cystoid ME (n = 57), diabetic ME (n = 86), or "mixed" (n = 10). We used advanced machine learning algorithms to develop a predictive classifier using the smallest number of parameters.

RESULTS:

Most differentiating were the existence of hard exudates, hyperreflective foci, subretinal fluid, ME pattern, and the location of cysts within retinal layers. Using only 3 to 6 spectral domain optical coherence tomography parameters, we achieved a sensitivity of 94% to 98%, specificity of 94% to 95%, and an area under the curve of 0.937 to 0.987 (depending on the method) for confirming a diabetic etiology. A simple decision flowchart achieved a sensitivity of 96%, a specificity of 95%, and an area under the curve of 0.937.

CONCLUSIONS:

Confirming a diabetic etiology for edema in cases with uncertainty between diabetic diabetic cystoid ME and pseudophakic ME was possible using few spectral-domain optical coherence tomography parameters with high accuracy. We propose a clinical decision flowchart for cases with uncertainty, which may support the decision for intravitreal injections rather than topical treatment.

Extensive circumferential partial-thickness sclerectomy in eyes with extreme nanophthalmos and spontaneous uveal effusion.

Mansour A, Stewart MW, Shields CL, Hamam R, Abdul Fattah M, Sheheitli H, Mehanna CJ, Yassine S, Chahine H, Keaik M, Maalouf F, Jaroudi M.

ABSTRACT

AIM:

To describe an extensive scleral excision technique to treat uveal effusion in nanophthalmic eyes.

METHODS:

This prospective, interventional series of eight eyes of five consecutive patients with nanophthalmos underwent scleral window surgeries. Ninety per cent of the scleral thickness, extending from immediately behind the extraocular muscle insertions to the vortex veins for 3 and 1/4 quadrants, was removed. The main outcome measure was resolution of the uveal effusions.

RESULTS:

Eight eyes of five patients (one female and four male) with a mean age of 46 years were studied. The mean (range) axial length was 16.1 mm (14.6-17.6 mm), and the mean refractive error was +13.6 dioptres (+10.75 to +16.00 dioptres). Following scleral excision surgery, all uveal effusions resolved within an average (±SD) of 13.9 (±8.7) days. The uveal effusion recurred in only one eye that had a vasoproliferative retinal tumour. The mean best corrected visual acuity improved from 0.69 logarithm of the minimum angle of resolution (logMAR) (Snellen equivalent: 20/97) at baseline to 0.51 logMAR (Snellen equivalent: 20/64; Wilcoxon paired t-test: p=0.016) after a mean follow-up of 35.6 months.

CONCLUSION:

 The circumferential scleral window technique produces rapid resolution of uveal effusion in nanophthalmic eyes. No adverse effects were noted after surgery and the clinical effect was durable through 1 year.

Outcomes of small-gauge vitreoretinal surgery without scleral-depressed shaving of the vitreous base in the era of wide-angle viewing systems.

Tabandeh H, London NJS, Boyer DS, Flynn HW Jr.

ABSTRACT

PURPOSE:

To evaluate outcomes of small-gauge pars plana vitrectomy (PPV) for the treatment of rhegmatogenous retinal detachment (RD) without scleral-depressed shaving of the vitreous base.

METHODS:

Retrospective, consecutive case series. Surgical technique included small-gauge PPV (25G, 23G, 25G+ or 27G) and wide-angle vitrectomy viewing system in all cases. No cases were excluded based on the level of complexity of RD. Outcome measures were retinal reattachment rates and Snellen visual acuity (best-corrected visual activity [BCVA])

RESULTS:

312 eyes of 301 patients, mean age 60.8 years, and mean follow-up 23.1 months. Baseline characteristics included macula-off RD in 207 (66%) eyes, psudophakia in 124 (40%) eyes, high myopia in 74 (24%) eyes and giant retinal tear in 14 (5%) eyes. The retina was reattached with one procedure in 296 (95%) eyes. Final retinal reattachment was achieved in 310 (99%) eyes. The BCVA at baseline was >20/40 in 76 (24%) eyes, 20/50-20/100 in 48 (15%) eyes, 20/200-20/400 in 46 (15%) eyes and <20/400 in 142 (46%) eyes. At the last follow-up, the BCVA was >20/40 in 168 (54%) eyes, 20/50-20/100 in 60 (19%) eyes, 20/200-20/400 in 49 (16%) eyes and <20/400 in 35 (11%) eyes. The mean change in logMAR equivalent was -0.12 for the macula-on group and -1.13 for the macula-off group (p<0.0001).

CONCLUSIONS:

Small-gauge PPV without scleral-depressed vitreous base shaving can be associated with good anatomical and visualoutcomes. Case selection based on the complexity of RD may not be required when considering small-gauge PPV.