Original Article

Coats disease in 351 eyes: Analysis of features and outcomes over 45 years (by decade) at a single center

Carol L Shields[1], Sanika Udyaver[1], Lauren A Dalvin[1,2], Li-Anne S Lim[1], Hatice T Atalay[1], Chloe T L Khoo[1], Mehdi Mazloumi[1], Jerry A Shields[1]

Purpose: To assess features and outcomes of Coats disease over 5-decades. **Methods:** Retrospective review of Coats disease patients at a single center. Features and outcomes were compared based on decade of presentation. **Results:** There were 351 patients with Coats disease. The presenting median age (6 years), male sex (84%), and unilaterality (100%) did not change per decade. Coats disease classification did not change per decade with Stage 1 (1%), Stage 2 (21%), Stage 3 (68%), Stage 4 (6%), and Stage 5 (1%). Clinical features that changed per decade (1970s vs. 1980s vs. 1990s vs. 2000s vs. 2010s) included 1980s features of more eyes with exudation in all 4 quadrants (22% vs. 58% vs. 44% vs. 33% vs. 27, $P = 0.01$) and total exudative retinal detachment (33% vs. 53% vs. 39% vs. 27% vs. 21%, $P < 0.001$). Imaging features that changed per decade included 2010s greater fluorescein angiographic extent of retinal non-perfusion in mean clock hours (4 vs. 4 vs. 3 vs. 5 vs. 6, $P = 0.003$), and 1980s greater mean height of retinal detachment ultrasonographically (5 vs. 12 vs. 5 vs. 5 vs. 4 mm, $P < 0.001$). Treatment features that changed per decade included 1980s greater primary enucleation (11% vs. 16% vs. 3% vs. 4% vs. 1%, $P = 0.001$), and 2010s greater use of laser photocoagulation (55% vs. 33% vs. 38% vs. 40% vs. 72%, $P < 0.001$), sub-Tenon corticosteroid (0% vs. 4% vs. 5% vs. 8% vs. 29%, $P < 0.001$), and intravitreal anti-VEGF) (0% vs. 4% vs. 2% vs. 13% vs. 18%, $P = 0.003$). Outcomes that changed per decade included 2010s findings of more complete resolution of subretinal fluid (64% vs. 59% vs. 38% vs. 58% vs. 72%, $P = 0.01$) and less need for primary/secondary enucleation (17% vs. 27% vs. 14% vs. 13% vs. 6%, $P = 0.04$). **Conclusion:** Eyes with Coats disease in the 1980s demonstrated more advanced findings, often requiring enucleation. Over the decades, greater use of laser photocoagulation and injections has led to improved disease resolution with greater globe salvage.

Key words: Coats disease, cryotherapy, enucleation, exudation, eye, laser photocoagulation, retina, surgery, telangiectasia

Access this article online

Website: www.ijo.in

DOI: 10.4103/ijo.IJO_449_19

Quick Response Code:

Coats disease is a retinal vasculopathy characterized by retinal telangiectasia, micro- and macro- retinal aneurysms, intra- and subretinal exudation, and exudative retinal detachment. This condition typically manifests in children, but can occasionally be found in adults, and in both situations, this vasculopathy can threaten visual acuity. In 2001, a classification for Coats disease was established, based on clinical features in 150 consecutive cases at a single center and with the goal of establishing guidelines for treatment and prediction of globe salvage and visual acuity outcomes.[1,2] This Coats disease classification included Stage 1 (retinal telangiectasia), Stage 2 (additional retinal exudation), Stage 3 (additional subretinal fluid), Stage 4 (additional total retinal detachment with neovascular glaucoma), and Stage 5 (endstage pre-phthisis bulbi or phthisis bulbi).[1] Further subdivision of stages 2 and 3 was provided to better assess extent and location of exudation and subretinal fluid. Since then, there have been several cohorts from India, Saudi Arabia, Turkey, Switzerland, United States, and other international centers analyzed based on this classification.[3-8]

In recent years, we have noted more sophisticated treatment of Coats disease with vitreoretinal or subretinal/external drainage surgery, laser photocoagulation, and periocular and/or intravitreal medications leading to a reduction in the need for enucleation, especially in advanced-stage Coats disease.[9-18] Herein, we provide a comprehensive overview of our 45-year experience with Coats disease diagnosis and management. We compare, by decade, the clinical and imaging features, management, and outcomes in 351 consecutive cases based on Coats disease classification.

[1]Ocular Oncology Service, Wills Eye Hospital, Thomas Jefferson University, 840 Walnut Street, 14th Floor, Philadelphia, PA, [2]Department of Ophthalmology, Mayo Clinic, Rochester, MN, 55905, USA

Support provided in part by the Eye Tumor Research Foundation, Philadelphia, PA (CLS). The funders had no role in the design and conduct of the study, in the collection, analysis and interpretation of the data, and in the preparation, review or approval of the manuscript. Carol L. Shields, M.D. has had full access to all the data in the study and takes responsibility for the integrity of the data.

Correspondence to: Dr. Carol L Shields, Ocular Oncology Service, 840 Walnut Street, Suite 1440, Philadelphia, PA 19107, USA. E-mail: carolshields@gmail.com

Manuscript received: 05.03.19; Revision accepted: 24.04.19

Cite this article as: Shields CL, Udyaver S, Dalvin LA, Lim LS, Atalay HT, Khoo CT, *et al.* Coats disease in 351 eyes: Analysis of features and outcomes over 45 years (by decade) at a single center. Indian J Ophthalmol 2019;67:772-83.

Methods

The medical, photographic, and imaging records of all patients diagnosed with Coats disease on the Ocular Oncology Service, Wills Eye Hospital, Philadelphia, PA from November 1, 1973 to July 31, 2018 were retrospectively reviewed. Patients with uncertain or alternative diagnoses were excluded. The records were then categorized based on decade at the time of presentation including 1973-1979 (1970s), 1980-1989 (1980s), 1990-1999 (1990s), 2000-2009 (2000s), 2010-2018 (2010s). The patient demographics, clinical features, imaging features, treatment modalities, and outcomes were then compared per decade.

Demographic data included age at presentation, race, sex, disease laterality, and study eye. Clinical features included presenting visual acuity (verbal or pre-verbal acuity), intraocular pressure (IOP) in mm Hg, Coats disease stage, presence, location, and extent of telangiectasia, aneurysms (light bulb), exudation, and subretinal fluid. Secondary anterior segment features included presence of xanthocoria, strabismus, corneal edema, anterior chamber cholesterolosis, iris neovascularization, iris atrophy, cataract, and phthisis bulbi.

Coats disease staging was based on a previously published classification as Stage 1 (only retinal telangiectasias), Stage 2A, (telangiectasia and extrafoveal exudation), Stage 2B (telangiectasia and foveal exudation), Stage 3A1 (subtotal extrafoveal exudative retinal detachment), Stage 3A2 (subtotal exudative retinal detachment involving the fovea), Stage 3B (total exudative retinal detachment), Stage 4 (total exudative retinal detachment and secondary glaucoma), or Stage 5 (advanced end-stage disease, phthisis bulbi).[1,19] Previously-treated patients who were referred with partially or completely resolved disease were characterized as unknown for staging.

Imaging features included fluorescein angiography documentation of location and extent of telangiectasia, light bulb aneurysms, retinal non-perfusion, cystoid macular edema, and neovascularization of optic disc, retina, and iris; optical coherence tomography (OCT), documentation of cystoid macular edema, epiretinal membrane, vitreomacular traction, subretinal/intraretinal fluid or exudation, central macular thickness and subfoveal choroidal thickness; ultrasonography documentation of presence and extent of retinal detachment, retinal elevation (mm height), and subretinal exudation. Treatment features included use of observation, laser photocoagulation, cryotherapy, sub-Tenon's or intravitreal corticosteroid, intravitreal anti-vascular endothelial growth factor (anti-VEGF), or enucleation. The number of non-enucleation therapies were counted.

Outcomes included visual acuity, amblyopia patching, and resolution of disease in general and specifically with regard to telangiectasia, exudation, and subretinal fluid. Further outcomes included development of iris neovascularization, glaucoma, traction retinal detachment and need for pars plana vitrectomy or enucleation and time to enucleation.

Data were tabulated in Microsoft Excel 2016 and analyzed using SPSS software (version 18 for Windows; SPSS Inc., Chicago, IL, USA). Continuous variables are expressed as mean (median, range). Comparison of eyes of each decade was performed using Student sample t-test for continuous variables and Chi-square or Fisher's exact test for categorical variables. The mean time to enucleation was calculated per each decade.

Table 1: Coats disease by decade in 351 eyes of 351 patients. Demographic characteristics

Demographic features	1973-1979 *n*=18 eyes in 18 patients (%)	1980-1989 *n*=43 eyes in 43 patients (%)	1990-1999 *n*=66 eyes in 66 patients (%)	2000-2009 *n*=112 eyes in 112 patients (%)	2010-2018 *n*=112 eyes in 112 patients (%)	*P*	Total *n*=351 eyes in 351 patients (%)
Age at presentation (years) Mean (median, range)	17 (10, 1-63)	10 (5, 0-59)	11 (5, 0-65)	11 (5, 0-64)	14 (8, 1-79)	0.38	12 (6, 0-79)
Race							
Caucasian	13 (72)	36 (84)	51 (77)	80 (71)	73 (65)		253 (72)
African American	3 (17)	4 (9)	8 (12)	18 (16)	21 (19)		54 (15)
Asian	0 (0)	0 (0)	2 (3)	2 (19)	5 (4)		9 (26)
Hispanic	2 (11)	2 (5)	4 (6)	12 (11)	8 (7)	0.59	28 (8)
Middle Eastern	0 (0)	0 (0)	1 (1)	0 (0)	2 (2)		3 (1)
Indian	0 (0)	1 (2)	0 (0)	0 (0)	3 (3)		4 (1)
Unknown	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)		0 (0)
Sex							
Male	16 (89)	33 (77)	57 (86)	95 (85)	95 (85)	0.66	296 (84)
Female	2 (11)	10 (23)	9 (14)	17 (15)	17 (15)		55 (16)
Laterality							
Unilateral	18 (100)	43 (100)	66 (100)	112 (100)	112 (100)	NA	351 (100)
Bilateral	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)		0 (0)
Study eye							
Right eye	4 (22)	21 (49)	32 (48)	55 (49)	51 (46)	0.31	163 (46)
Left eye	14 (78)	22 (51)	34 (52)	57 (51)	61 (54)		188 (54)

Bold values indicate significant *P*

Table 2: Coats disease by decade in 351 eyes of 351 patients. Clinical characteristics

Clinical features	1973-1979 *n*=18 eyes in 18 patients (%)	1980-1989 *n*=43 eyes in 43 patients (%)	1990-1999 *n*=66 eyes in 66 patients (%)	2000-2009 *n*=112 eyes in 112 patients (%)	2010-2018 *n*=112 eyes in 112 patients (%)	*P*	Total *n*=351 eyes in 351 patients (%)
Visual acuity							
Verbal visual acuity							
≥20/40	1 (6)	1 (2)	6 (9)	18 (16)	26 (23)		52 (15)
20/50-20/200	6 (33)	11 (26)	13 (20)	21 (19)	20 (18)	0.10	71 (20)
<20/200	5 (28)	15 (35)	20 (30)	36 (32)	42 (38)		118 (34)
Preverbal visual acuity							
Fix and follow	0 (0)	0 (0)	5 (8)	9 (8)	5 (5)		19 (5)
Poor fix and follow	3 (17)	1 (2)	2 (3)	2 (2)	8 (7)	**0.01**	16 (5)
No fix and follow	3 (17)	14 (33)	17 (26)	25 (22)	11 (10)		70 (20)
Uncooperative	0 (0)	1 (2)	3 (5)	1 (1)	0 (0)		5 (1)
Intraocular pressure Mean (median, range)	16 (15, 7-48)	21 (15, 7-60)	16 (15, 6-26)	16 (15, 10-36)	16 (15, 6-40)	**0.001**	16 (15, 6-60)
Coats disease stage (complete)							
1	0 (0)	0 (0)	0 (0)	2 (2)	3 (3)		5 (1)
2a	2 (11)	1 (2)	8 (12)	6 (5)	14 (13)		31 (9)
2b	4 (22)	6 (14)	10 (15)	14 (13)	8 (7)		42 (12)
3a1	2 (11)	3 (7)	10 (15)	18 (16)	13 (12)	0.09	46 (13)
3a2	3 (17)	8 (19)	10 (15)	25 (22)	22 (20)		68 (19)
3b	6 (33)	18 (42)	24 (36)	40 (36)	37 (33)		125 (36)
4	1 (6)	7 (16)	3 (5)	5 (4)	4 (4)		20 (6)
5	0 (0)	0 (0)	0 (0)	1 (1)	2 (2)		3 (1)
Unknown*	0 (0)	0 (0)	1 (2)	1 (1)	9 (8)		11 (3)
Coats disease simplified stage							
1	0 (0)	0 (0)	0 (0)	2 (2)	3 (3)	0.53	5 (1)
2	6 (33)	7 (16)	18 (27)	20 (18)	22 (20)	0.33	73 (21)
3	11 (61)	29 (67)	44 (67)	83 (74)	72 (64)	0.54	239 (68)
4	1 (6)	7 (16)	3 (4)	5 (4)	4 (4)	**0.03**	20 (6)
5	0 (0)	0 (0)	0 (0)	1 (1)	2 (2)	0.69	3 (1)
Telangiectasia							
Telangiectasia clock hours Mean (median, range)	5 (4, 2-12)	6 (5, 0-12)	5 (3, 0-12)	6 (5, 0-12)	5 (5, 0-12)	0.28	5 (5, 0-12)
Telangiectasia quadrants							
0	0 (0)	1 (2)	3 (5)	3 (3)	9 (8)		16 (5)
1	6 (33)	15 (35)	28 (42)	30 (27)	28 (25)		107 (30)
2	8 (44)	11 (26)	13 (20)	28 (25)	37 (33)	0.13	97 (28)
3	1 (6)	7 (2)	14 (21)	27 (18)	14 (13)		63 (18)
4	2 (11)	8 (19)	8 (12)	20 (18)	17 (15)		55 (16)
No view**	1 (6)	1 (2)	0 (0)	4 (4)	7 (6)		13 (4)
Location of most telangiectasia							
Equator to ora serrata	14 (78)	28 (65)	36 (55)	81 (72)	68 (61)		227 (65)
Macula to equator	3 (17)	12 (28)	26 (39)	24 (21)	28 (25)		93 (26)
Macula	0 (0)	1 (2)	1 (2)	0 (0)	0 (0)	0.11	2 (1)
None	0 (0)	1 (2)	3 (5)	3 (3)	9 (8)		16 (5)
No view**	1 (6)	1 (2)	0 (0)	4 (4)	7 (6)		13 (4)
Light bulb aneurysms							
Light bulb clock hours Mean (median, range)	4 (3, 2-12)	5 (3, 0-12)	4 (3, 0-12)	5 (4, 0-12)	4 (4, 0-12)	0.24	5 (4, 0-12)

Contd...

Table 2: Contd...

Clinical features	1973-1979 *n*=18 eyes in 18 patients (%)	1980-1989 *n*=43 eyes in 43 patients (%)	1990-1999 *n*=66 eyes in 66 patients (%)	2000-2009 *n*=112 eyes in 112 patients (%)	2010-2018 *n*=112 eyes in 112 patients (%)	*P*	Total *n*=351 eyes in 351 patients (%)
Light bulb quadrants							
0	0 (0)	5 (12)	11 (17)	10 (9)	14 (13)		40 (11)
1	8 (44)	17 (2)	26 (29)	30 (27)	31 (28)		112 (32)
2	8 (4)	9 (21)	12 (18)	31 (28)	40 (36)	0.05	100 (28)
3	0 (0)	4 (9)	11 (17)	19 (17)	8 (7)		42 (12)
4	1 (6)	7 (16)	6 (9)	18 (16)	12 (11)		44 (13)
No view**	1 (6)	1 (2)	0 (0)	4 (4)	7 (6)		13 (4)
Location of most light bulbs							
Equator to ora serrata	14 (78)	26 (60)	34 (52)	73 (65)	69 (62)		216 (62)
Macula to equator	3 (17)	11 (26)	20 (30)	24 (21)	22 (20)		80 (23)
Macula	0 (0)	0 (0)	1 (1)	1 (1)	0 (0)	0.52	2 (1)
None	0 (0)	5 (12)	11 (17)	10 (9)	14 (13)		40 (11)
No view**	1 (6)	1 (2)	0 (0)	4 (4)	7 (6)		13 (4)
Exudation							
Exudation clock hours Mean (median, range)	7 (6, 2-12)	9 (12, 0-12)	8 (9, 0-12)	7 (7, 0-12)	6 (6, 0-12)	**0.01**	7 (7, 0-12)
Exudation quadrants							
0	0 (0)	0 (0)	1 (2)	4 (4)	7 (6)		12 (3)
1	3 (17)	5 (12)	11 (17)	13 (12)	23 (21)		55 (16)
2	6 (33)	11 (26)	13 (20)	32 (29)	34 (30)	**0.01**	96 (27)
3	5 (28)	1 (2)	12 (18)	23 (21)	11 (10)		52 (15)
4	4 (22)	25 (58)	29 (44)	37 (33)	30 (27)		125 (36)
No view**	0 (0)	1 (2)	0 (0)	3 (3)	7 (6)		11 (3)
Location of most exudation							
Equator to ora serrata	0 (0)	3 (7)	10 (15)	12 (11)	14 (13)		39 (11)
Macula to equator	11 (61)	24 (56)	35 (53)	52 (46)	39 (35)		161 (46)
Macula	7 (39)	15 (35)	20 (30)	41 (37)	45 (40)	0.20	128 (36)
None	0 (0)	0 (0)	1 (2)	4 (4)	7 (6)		12 (3)
No view**	0 (0)	1 (2)	0 (0)	3 (3)	7 (6)		11 (3)
Subretinal fluid							
Subretinal fluid clock hours Mean (median, range)	6 (5, 0-12)	8 (12, 0-12)	7 (7, 0-12)	7 (7, 0-12)	6 (5, 0-12)	0.11	7 (6, 0-12)
Subretinal fluid quadrants							
0	4 (22)	3 (7)	8 (12)	12 (11)	26 (23)		53 (15)
1	3 (17)	9 (21)	13 (29)	24 (21)	14 (13)		63 (18)
2	3 (17)	6 (14)	9 (14)	16 (14)	22 (20)	**0.02**	56 (16)
3	1 (6)	0 (0)	8 (12)	15 (13)	4 (4)		28 (8)
4	7 (29)	24 (56)	28 (42)	43 (38)	39 (35)		141 (40)
No view**	0 (0)	1 (2)	0 (0)	2 (2)	7 (6)		10 (3)
Location of most subretinal fluid							
Equator to ora serrata	3 (17)	3 (7)	8 (12)	15 (13)	18 (16)		47 (13)
Macula to equator	5 (28)	7 (16)	20 (30)	44 (39)	31 (28)		107 (30)
Macula	0 (0)	5 (12)	5 (8)	2 (2)	3 (3)	**0.002**	15 (4)
Total retinal detachment	6 (33)	24 (56)	25 (8)	37 (33)	27 (24)		119 (34)
None	4 (22)	3 (7)	8 (12)	12 (11)	26 (23)		53 (15)
No view**	0 (0)	1 (2)	0 (0)	2 (2)	7 (6)		10 (3)
Most posterior extent of disease							
Ora serrata	0 (0)	0 (0)	1 (2)	3 (3)	2 (2)		6 (2)

Contd...

Table 2: Contd...

Clinical features	1973-1979 *n*=18 eyes in 18 patients (%)	1980-1989 *n*=43 eyes in 43 patients (%)	1990-1999 *n*=66 eyes in 66 patients (%)	2000-2009 *n*=112 eyes in 112 patients (%)	2010-2018 *n*=112 eyes in 112 patients (%)	*P*	Total *n*=351 eyes in 351 patients (%)
Equator	1 (6)	1 (2)	3 (5)	10 (9)	24 (21)		39 (11)
Arcade	2 (11)	4 (9)	17 (26)	24 (21)	19 (17)	**<0.001**	66 (19)
Macula	1 (6)	6 (14)	7 (11)	27 (24)	27 (24)		68 (19)
Fovea	8 (33)	8 (19)	12 (18)	15 (13)	9 (8)		52 (15)
Total retinal detachment	6 (33)	23 (53)	26 (39)	30 (27)	24 (21)		109 (31)
No view**	0 (0)	1 (2)	0 (0)	3 (3)	7 (7)		11 (3)
Posterior segment findings, other							
Vitreoretinal traction	0 (0)	3 (7)	6 (9)	9 (8)	10 (9)	0.74	28 (8)
Neovascularization of the disc	0 (0)	1 (2)	0 (0)	0 (0)	1 (1)	0.45	2 (1)
Neovascularization of the retina	1 (6)	1 (2)	0 (0)	1 (1)	3 (3)	0.41	6 (2)
Retinal hemorrhage	2 (11)	6 (14)	12 (18)	15 (13)	10 (9)	0.59	45 (13)
Vitritis	1 (6)	1 (2)	1 (2)	2 (2)	0 (0)	0.41	5 (1)
Anterior segment findings							
Xanthocoria	5 (28)	15 (35)	18 (27)	45 (40)	49 (44)	0.20	132 (38)
Strabismus	5 (28)	20 (47)	17 (26)	38 (34)	31 (27)	0.16	111 (31)
Corneal edema	1 (6)	1 (2)	0 (0)	0 (0)	2 (2)	0.19	4 (1)
Anterior chamber cholesterolosis	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0.36	1 (0.2)
Iris neovascularization	1 (6)	6 (14)	5 (8)	7 (6)	5 (4)	0.33	24 (7)
Iris atrophy	1 (6)	1 (2)	0 (0)	1 (1)	1 (1)	0.34	4 (1)
Cataract	1 (6)	1 (2)	1 (2)	7 (6)	7 (6)	0.53	17 (5)
Pthisis	0 (0)	0 (0)	0 (0)	0 (0)	1 (1)	0.71	1 (0.2)

Bold values indicate significant *P*, *Staging unknown for 11 eyes secondary to resolved disease at presentation (*n*=6) and media opacities (*n*=5), **No view secondary to media opacities (cataract, total serous retinal detachment), Intraocular pressure: *Post-hoc* analysis (Bonferroni test) showed significant differences between groups 2 and 3 (*P*=0.003), and 2 and 4 (*P*=0.001), and 2 and 5 (*P*<0.001). There was no significant difference between the means of the other groups (*P*>0.05). Exudation clock-hours: *Post-hoc* analysis (Bonferroni test), showed a significant difference between groups 2 and 5 (*P*=0.01). There was no significant difference between the means of the other groups (*P*>0.05)

Results

There were 351 eyes of 351 patients with Coats disease in this analysis. Based on decade of presentation, number of patients per decade included 1970s (n = 18, 5%), 1980s (n = 43, 12%) 1990s (n = 66, 18%) 2000s (n = 112, 32%), and 2010s (2010-2018) (n = 112, 32%).

The demographic features are listed in Table 1. Overall median age at presentation was 6 years, race was Caucasian (72%), sex was male (84%), involvement was unilateral (100%), and left eye was affected (54%). A comparison of demographic features over the decades (1970s vs. 1980s vs. 1990s vs. 2000s vs. 2010s) revealed no significant difference in presenting age, race, sex, laterality, or affected eye ($p > 0.05$).

The clinical features are listed in Table 2. A comparison of features by decade revealed a difference in pre-verbal visual acuity, with greater no fix and follow vision in the 1980s and less in the 2010s (17% vs. 33% vs. 26% vs. 22% vs. 10%, $P = 0.01$). There were several clinical features that predominated in the 1980s including greater mean intraocular pressure (16 vs. 21 vs. 16 vs. 16 vs. 16 mmHg, $P = 0.001$), greater mean clock hours of exudation (7 vs. 9 vs. 8 vs. 7 vs. 6, $P = 0.01$), and greater prevalence of 4 quadrants of exudation (22% vs. 58% vs. 44% vs. 33% vs. 27, $P = 0.01$), 4 quadrants of subretinal fluid (29% vs. 56% vs. 42% vs. 38% vs. 35%, $P = 0.02$), and total exudative retinal detachment (33% vs. 53% vs. 39% vs. 27% vs. 21%, $P < 0.001$). Per decade, there was no difference in verbal visual acuity, Coats disease stage (complete and simplified), telangiectasia (clock hours, quadrant, and location), light bulb aneurysms (clock hours, quadrant, and location), and other posterior and anterior segment findings of neovascularization of the optic disc, retina and iris.

The imaging features are listed in Table 3. A comparison of imaging features by decade revealed the 2010s with greater mean clock hours of peripheral non-perfusion (4 vs. 4 vs. 3 vs. 5 vs. 6, $P = 0.003$). There were several imaging features that predominated in the 1980s including greater presence of retinal detachment by ultrasonography (60% vs. 83% vs. 82% vs. 59% vs. 48%, $P = 0.01$), greater mean elevation of subretinal fluid by ultrasonography (5 vs. 12 vs. 5 vs. 5 vs. 4 mm, $P < 0.001$), and more prevalent closed funnel retinal detachment (0% vs. 33% vs. 7% vs. 7% vs. 9%, $P = 0.01$). Per decade, there was no difference in fluorescein angiographic documentation of telangiectasia (extent, location, and quadrant), light bulb aneurysm (extent, location, and quadrant), cystoid macular

Table 3: Coats disease by decade in 351 eyes of 351 patients. Imaging features

Imaging features	1973-1979 *n*=18 eyes in 18 patients (%)	1980-1989 *n*=43 eyes in 43 patients (%)	1990-1999 *n*=66 eyes in 66 patients (%)	2000-2009 *n*=112 eyes in 112 patients (%)	2010-2018 *n*=112 eyes in 112 patients (%)	*P*	Total *n*=351 eyes in 351 patients (%)
Fluorescein angiography*	*n*=4	*n*=17	*n*=26	*n*=58	*n*=87		*n*=192
Telangiectasia							
Clock hours Mean (median, range)	3 (4, 2-4)	5 (5, 1-12)	5 (5, 0-12)	6 (6, 0-12)	6 (6, 0-12)	0.38	6 (6, 0-12)
Most affected region							
Temporal	3 (75)	12 (71)	18 (69)	43 (74)	69 (79)		145 (76)
Nasal	0 (0)	3 (18)	2 (8)	1 (2)	7 (8)		13 (7)
Inferior	1 (25)	1 (6)	4 (15)	9 (16)	4 (5)	0.55	19 (10)
Superior	0 (0)	1 (6)	1 (4)	3 (5)	6 (7)		11 (6)
No telangiectasia	0 (0)	0 (0)	1 (4)	2 (3)	1 (1)		4 (2)
Most affected quadrant							
Superonasal	0 (0)	1 (6)	2 (8)	2 (3)	6 (7)		11 (6)
Superotemporal	1 (25)	5 (29)	5 (19)	20 (34)	32 (37)		63 (32)
Inferonasal	0 (0)	3 (18)	5 (19)	2 (3)	5 (6)	0.58	15 (8)
Inferotemporal	3 (75)	8 (47)	13 (50)	32 (55)	43 (49)		99 (52)
No telangiectasia	0 (0)	0 (0)	1 (3)	2 (3)	1 (1)		4 (2)
Light bulb aneurysms							
Clock hours Mean (median, range)	3 (4, 2-4)	4 (3, 0-12)	5 (3, 0-12)	5 (4, 0-12)	5 (5, 0-12)	0.40	5 (5, 0-12)
Most affected region							
Temporal	3 (75)	11 (65)	17 (65)	41 (71)	65 (75)		137 (71)
Nasal	0 (0)	3 (18)	2 (8)	1 (2)	5 (6)		11 (6)
Inferior	1 (25)	1 (6)	4 (15)	9 (16)	6 (7)	0.72	21 (11)
Superior	0 (0)	1 (6)	1 (4)	3 (5)	7 (8)		12 (6)
No light bulb aneurysms	0 (0)	1 (6)	2 (8)	4 (7)	4 (5)		11 (6)
Most affected quadrant							
Superonasal	1 (25)	1 (6)	2 (8)	1 (2)	8 (9)		13 (7)
Superotemporal	0 (0)	5 (29)	6 (23)	19 (33)	28 (32)		48 (22)
Inferonasal	0 (0)	3 (18)	2 (8)	2 (3)	3 (3)	0.53	10 (5)
Inferotemporal	3 (75)	7 (41)	14 (54)	32 (55)	44 (51)		100 (52)
No light bulb aneurysms	0 (0)	1 (6)	2 (7)	4 (7)	4 (5)		11 (6)
Retinal non-perfusion							
Clock hours Mean (median, range)	4 (5, 2-6)	4 (3, 0-12)	3 (3, 0-12)	5 (4, 0-12)	6 (6, 0-12)	**0.003**	5 (5, 0-12)
Most affected region							
Temporal	4 (100)	10 (59)	14 (54)	31 (53)	62 (71)		121 (63)
Nasal	0 (0)	2 (12)	2 (8)	1 (2)	7 (8)		12 (6)
Inferior	0 (0)	0 (0)	3 (12)	5 (9)	5 (6)	0.23	13 (7)
Superior	0 (0)	1 (6)	0 (0)	4 (7)	4 (5)		9 (5)
No non-perfusion	0 (0)	4 (24)	7 (27)	17 (29)	9 (10)		37 (19)
Most affected quadrant							
Superonasal	0 (0)	1 (6)	2 (8)	2 (3)	6 (7)		11 (6)
Superotemporal	1 (25)	5 (29)	5 (19)	18 (31)	29 (33)		58 (30)
Inferonasal	0 (0)	1 (6)	2 (8)	1 (2)	2 (2)	0.43	6 (3)
Inferotemporal	3 (75)	6 (35)	10 (38)	20 (34)	41 (47)		80 (42)
No non-perfusion	0 (0)	4 (24)	7 (27)	17 (29)	9 (10)		37 (19)
Other fluorescein features							
Cystoid macular edema	0 (0)	0 (0)	2 (8)	8 (14)	9 (10)	0.49	19 (10)
Neovascularization of the disc	0 (0)	0 (0)	1 (4)	0 (0)	1 (1)	0.59	2 (1)
Neovascularization of the retina	0 (0)	0 (0)	1 (4)	2 (3)	2 (2)	0.92	5 (3)
Neovascularization of the iris	0 (0)	0 (0)	1 (4)	5 (9)	5 (6)	0.67	11 (3)

Contd...

Table 3: Contd...

Imaging features	1973-1979 *n*=18 eyes in 18 patients (%)	1980-1989 *n*=43 eyes in 43 patients (%)	1990-1999 *n*=66 eyes in 66 patients (%)	2000-2009 *n*=112 eyes in 112 patients (%)	2010-2018 *n*=112 eyes in 112 patients (%)	*P*	Total *n*=351 eyes in 351 patients (%)
Optical coherence tomography**	*n*=0	*n*=0	*n*=0	*n*=41	*n*=81		*n*=122
Cystoid macular edema	NA	NA	NA	17 (42)	21 (26)	0.13	38 (31)
Epiretinal membrane	NA	NA	NA	13 (32)	17 (21)	0.27	30 (24)
Vitreomacular traction	NA	NA	NA	4 (10)	6 (7)	0.73	10 (8)
Subretinal fluid	NA	NA	NA	22 (54)	38 (47)	0.71	60 (49)
Subretinal exudation	NA	NA	NA	36 (88)	59 (73)	0.18	95 (78)
Intraretinal exudation	NA	NA	NA	10 (24)	20 (25)	0.82	30 (25)
Central macular thickness (um) Mean (median, range)	NA	NA	NA	349 (313, 176-647)	363 (343, 191-692)	0.46	358 (336, 176-692)
Foveal center to RPE thickness (um) Mean (median, range)	NA	NA	NA	358 (279, 213-992)	351 (301, 0-956)	0.90	352 (200, 0-992)
Foveal center to base of retina (um) Mean (median, range)	NA	NA	NA	255 (247, 188-342)	302 (251, 0-918)	0.38	293 (252, 0-918)
Subfoveal choroid thickness (um) Mean (median, range)	NA	NA	NA	207 (211, 96-288)	294 (295, 0-630)	**0.01**	279 (282, 0-630)
Ultrasonography†	*n*=5	*n*=18	*n*=28	*n*=83	*n*=82		*n*=216
Retinal detachment	3 (60)	15 (83)	23 (82)	49 (59)	39 (48)	**0.01**	129 (60)
Partial retinal detachment	0 (0)	0 (0)	2 (7)	9 (11)	6 (7)	0.69	17 (8)
Total retinal detachment	1 (20)	1 (6)	2 (7)	6 (7)	11 (13)	0.55	21 (10)
Open funnel detachment	2 (40)	8 (44)	17 (61)	28 (28)	15 (18)	**0.001**	70 (32)
Closed funnel detachment	0 (0)	6 (33)	2 (7)	6 (7)	7 (9)	**0.01**	21 (10)
Subretinal fluid elevation (mm) Mean (median, range)	5 (2, 0-19)	12 (16, 0-19)	5 (4, 0-16)	5 (2, 0-19)	4 (0, 0-18)	**<0.001**	5 (2, 0-19)
Subretinal exudation	5 (100)	17 (94)	27 (96)	77 (93)	69 (84)	0.19	195 (90)

Bold values indicate significant *P*. *Fluorescein angiography available in 201 eyes **Optical coherence tomography available in 122 eyes †Ultrasonography available in 225 eyes Abbreviations: NA=not applicable Non-perfusion clock hours on fluorescein angiography: *Post-hoc* analysis (Bonferroni test) showed a significant difference between groups 3 and 5 (*P*=0.01). There was no significant difference between the means of any other groups (*P*>0.05). Subretinal fluid elevation (mm) on ultrasound: *Post-hoc* analysis (Bonferroni test) showed significant differences between groups 2 and 3 (*P*=0.001), groups 2 and 4 (*P*<0.001), and groups 2 and 5 (*P*<0.001). There was no significant difference between the means of any other groups (*P*>0.05)

edema, and neovascularization of the optic disc, retina, and iris.

The treatment features are listed in Table 4. A comparison of treatment features by decade revealed several features in the 2010s with less frequent management with observation (39% vs. 21% vs. 33% vs. 21% vs. 11%, $P = 0.002$), greater total number of treatments (2.9 vs. 2.0 vs. 1.8 vs. 3.6 vs. 4.5, $P = 0.001$), and more use of argon laser photocoagulation (55% vs. 33% vs. 38% vs. 40% vs. 72%, $P < 0.001$), sub-Tenon corticosteroid injection (0% vs. 4% vs. 5% vs. 8% vs. 29%, $P < 0.001$), and intravitreal anti-VEGF (0% vs. 4% vs. 2% vs. 13% vs. 18%, $P = 0.003$). Fewer eyes in the 2010s were treated with primary enucleation (11% vs. 16% vs. 3% vs. 4% vs. 1%, $P = 0.001$). Per decade, there was no difference in cryotherapy use.

The outcomes are listed in Table 5. A comparison of outcomes by decade revealed longer follow-up for patients who presented in the 1970s (118 vs. 101 vs. 66 vs. 54 vs. 32 months, $P < 0.001$). Eyes from the 2010s had more complete disease resolution (58% vs. 45% vs. 37% vs. 55% vs. 73%, $P = 0.002$), more complete subretinal fluid resolution (64% vs. 59% vs. 38% vs. 58% vs. 72%, $P = 0.01$), and fewer overall need for primary or secondary enucleation (17% vs. 27% vs. 14% vs. 13% vs. 6%, $P = 0.04$). On sub-analysis with Fisher's exact test, disease resolution was more likely in eyes from the 2010s compared to eyes in the 1980s ($p = 0.01$) and 1990s ($p = 0.002$); subretinal fluid resolution was more likely in eyes from the 2010s compared to eyes in the 1990s ($p < 0.001$); and enucleation was less likely in patients seen in the 2010s compared to patients seen in the 1980s ($p = 0.003$). Per decade, there was no difference in development of iris neovascularization, traction retinal detachment, glaucoma, and need for pars plana vitrectomy.

Discussion

Coats disease represents a broad clinical spectrum of retinal vasculopathy, predominantly in children, and demonstrating telangiectasia, exudation, retinal detachment, and occasionally neovascular glaucoma or phthisis bulbi.[1-3,4-18] The management of Coats disease begins with documentation of the extent of vasculopathy using clinical examination and imaging, particularly with fluorescein angiography. When extensive exudation or retinal detachment is present, Coats disease can simulate malignant retinoblastoma. In a comprehensive analysis of 2781 patients referred with possible retinoblastoma, 604 (22%) had pseudoretinoblastoma, with the leading three conditions including Coats disease (n = 244, 40%), persistent fetal vasculature (PFV) (n = 158, 28%), and vitreous

Table 4: Coats disease by decade in 351 eyes of 351 patients. Treatment features

Treatment features	1973-1979 *n*=18 eyes in 18 patients (%)	1980-1989 *n*=43 eyes in 43 patients (%)	1990-1999 *n*=66 eyes in 66 patients (%)	2000-2009 *n*=112 eyes in 112 patients (%)	2010-2018 *n*=112 eyes in 112 patients (%)	*P*	Total *n*=351 eyes in 351 patients (%)
Observation	7 (39)	9 (21)	22 (33)	23 (21)	12 (11)	**0.002**	73 (21)
Medical or laser therapy	9 (50)	27 (63)	42 (64)	84 (75)	99 (88)	**<0.001**	261 (74)
Number of total treatments Mean (median, range)	2.9 (2, 1-6)	2.0 (1, 0-13)	1.8 (2, 1-4)	3.6 (3, 1-15)	4.5 (3, 1-26)	**0.001**	3.6 (3, 1-26)
Argon laser photocoagulation	5 (55)	9 (33)	16 (38)	45 (40)	71 (72)	**<0.001**	146 (42)
Number of treatments Mean (median, range)	2.0 (2, 1-4)	3.0 (2, 1-11)	1.2 (1, 1-2)	1.9 (2, 1-4)	2.3 (1, 1-20)	0.22	2.1 (1, 1-20)
Cryotherapy	7 (78)	25 (93)	30 (71)	65 (58)	67 (68)	0.20	194 (55)
Number of treatments Mean (median, range)	2.3 (2, 1-5)	2.0 (2, 1-6)	1.6 (1, 1-3)	2.3 (2, 1-9)	2.1 (2, 1-6)	0.22	2.1 (2, 1-9)
Sub-Tenon corticosteroid injection	0 (0)	1 (4)	2 (5)	9 (8)	29 (29)	**<0.001**	41 (12)
Number of treatments Mean (median, mode)	NA	1.0 (1, 1-1)	1.0 (1, 1-1)	1.7 (1, 1-4)	1.2 (1, 1-3)	0.24	1.3 (1, 1-4)
Intravitreal corticosteroid injection	0 (0)	0 (0)	1 (2)	4 (4)	9 (9)	0.08	14 (4)
Number of treatments Mean (median, range)	NA	NA	1.0 (1, 1-1)	1.8 (2, 1-3)	3.7 (1, 1-14)	0.67	2.9 (1, 1-26)
Anti-VEGF	0 (0)	1 (4)	1 (2)	15 (13)	18 (18)	**0.003**	35 (10)
Number of treatments Mean (median, range)	NA	0.1 (0, 0-3)	1.0 (1, 1-1)	2.7 (1, 1-12)	4.2 (2, 1-20)	0.72	3.4 (2, 1-20)
Primary enucleation	2 (11)	7 (16)	2 (3)	5 (4)	1 (1)	**0.001**	17 (5)
No follow-up	6 (33)	10 (23)	23 (35)	36 (32)	28 (25)	0.51	103 (29)

Bold values indicate significant *P*. *Other signifies less common treatments such as scleral buckle, photodynamic therapy, transpupillary thermotherapy, and plaque radiotherapy, NA=Not applicable, VEGF=Vascular endothelial growth factor, Number of total treatments: *Post-hoc* analysis (Bonferroni test) showed a significant difference between groups 3 and 5 (*P*<0.001). There was no significant difference between any other groups (*P*>0.05)

hemorrhage (n = 27, 5%), comprising 73% of the simulators.[20] In that analysis, based on age, pseudoretinoblastoma under the age of 1 year was most likely PFV (49%), whereas it was more likely Coats disease for those age 2-5 years (61%) and those older than 5 years (57%).[20] These simulating conditions can be sorted to the correct diagnosis with the recognition of classic clinical and imaging features like exudative retinal detachment, irregularly-dilated telangiectactic retinal vessels, and peripheral non-perfusion of Coats disease compared to serous retinal detachment, solid tumor with seeding, and tortuous, but smoothly-dilated retinal vessels of retinoblastoma.[9,19,21]

In this analysis, we reviewed our 45-year experience with Coats disease, decade-by-decade. We found that several factors have not changed over the years such as median patient age at 6 years, predominant race as Caucasian (72%), and sex as male (84%). Importantly, there was no difference in Coats disease stage (complete or simplified) over this period. However, there were a few features that changed over time, with significantly more advanced Coats disease in the 1980s, demonstrating higher intraocular pressure (p = 0.001), greater degree of exudation (p = 0.01) and subretinal fluid (p = 0.02), and more frequent total exudative retinal detachment (p < 0.001), all likely related to poorer entering verbal visual acuity (<20/200 (35%) P = 0.10) and preverbal visual acuity (no fix or follow (33%) P = 0.01). In fact, in the 1980s, exudative retinal detachment was significantly more highly elevated ultrasonographically (p < 0.001), a feature that has been subsequently correlated with need for enucleation.[22] Udyaver *et al*. studied features of Coats disease predictive of enucleation and found that each 1 millimeter increase in exudative retinal detachment thickness (by ultrasonography) increased the risk for enucleation by 20% (odds ration [OR] = 1.20) and each additional clock hour of light bulb aneurysms increased the risk by 35% (OR = 1.35).[22] Khoo *et al*. studied factors predictive of exudative retinal detachment resolution following treatment of eyes with Coats disease and noted that every 1 mm decrease in exudative retinal detachment elevation was associated with improved fluid resolution by 16%.[23]

Coats disease is typically discovered in the pediatric age group. In this analysis, the median age at presentation was 6 years and the mean age was 12 years (with range up to 79 years), maintained at a fairly steady level throughout the 5 decades. In 2001, a report from the United States (US) on 150 cases of Coats disease found median age at 5 years, mean age at 11 years with range up to 63 years, male prevalence at 76%, and unilaterality at 95%.[1,2] Later, in 2010, a population-based study from the United Kingdom (UK) on 55 cases revealed median age at 8 years and mean age at 12 years, again skewed by a small number of cases presenting in later adult life.[24] In the UK study, all cases were unilateral and 85% were male, as in our report. The estimated population-based incidence was 0.09/100,000 persons and they noted 44% of patients were blind (20/200 or worse) at diagnosis and younger patients demonstrated more severe stages of Coats disease.[24] They concluded that Coats disease in young patients have increased disease severity with poorer visual acuity.[24] Daruich *et al*. studied age of onset of Coats disease in 98 cases from

Table 5: Coats disease by decade in 351 eyes of 351 patients. Outcomes

Outcomes	1973-1979 *n*=12 eyes in 12 patients (%)	1980-1989 *n*=33 eyes in 33 patients (%)	1990-1999 *n*=43 eyes in 43 patients (%)	2000-2009 *n*=76 eyes in 76 patients (%)	2010-2018 *n*=84 eyes in 84 patients (%)	*P*	Total *n*=248 eyes in 248 patients (%)
Follow-up (months) Mean (median, range)	118 (62, 3-392)	101 (41, 0-466)	66 (17, 1-287)	54 (38, 0-194)	32 (29, 0-165)	**<0.001**	58 (31, 0-466)
Visual acuity							
Verbal visual acuity							
>20/40	0 (0)	3 (9)	5 (12)	9 (12)	20 (24)		37 (15)
20/50-20/200	3 (25)	6 (18)	3 (7)	13 (17)	20 (22)	0.13	45 (18)
<20/200	6 (50)	20 (61)	19 (44)	39 (51)	34 (40)		118 (48)
Preverbal visual acuity							
Fix and follow	0 (0)	0 (0)	1 (2)	1 (1)	1 (1)		3 (1)
Poor fix and follow	0 (0)	0 (0)	0 (0)	1 (1)	0 (0)	0.92	1 (0.4)
No fix and follow	0 (0)	2 (6)	7 (16)	9 (12)	4 (5)		22 (9)
No cooperation	3 (25)	2 (6)	8 (19)	4 (5)	5 (6)		22 (9)
If visual acuity (<20/200), cause for poor visual acuity	*n*=10	*n*=25	*n*=29	*n*=50	*n*=48		N=162
Macular scar	6 (60)	10 (40)	12 (41)	26 (52)	24 (5)		78 (48)
Persistent SRF	1 (10)	1 (4)	1 (3)	1 (2)	0 (0)		4 (2)
Loss of ellipsoid zone	0 (0)	0 (0)	1 (3)	4 (8)	8 (17)		13 (8)
Vitreoretinal traction	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0.16	1 (1)
Retinal detachment	3 (30)	12 (48)	14 (48)	18 (36)	15 (31)		62 (38)
Cataract	0 (0)	2 (8)	0 (0)	0 (0)	0 (0)		2 (1)
Macular hole	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)		1 (1)
Macular hemorrhage	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)		1 (1)
Poor visual acuity (<20/200) by Coats disease stage	*n*=10	*n*=25	*n*=29	*n*=50	*n*=48		*n*=162
1	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	NA	0 (0)
2	3 (30)	2 (8)	6 (21)	6 (12)	3 (6)	0.85	20 (12)
3	6 (60)	17 (68)	23 (79)	41 (82)	39 (81)	0.93	126 (78)
4	1 (10)	6 (24)	0 (0)	2 (4)	2 (4)	0.11	11 (7)
5	0 (0)	0 (0)	0 (0)	1 (2)	1 (2)	0.11	2 (1)
Unknown	0 (0)	0 (0)	0 (0)	0 (0)	3 (6)	0.92	3 (2)
Disease resolution							
Resolved	7 (58)	15 (45)	16 (37)	42 (84)	61 (73)	**0.002**	141 (57)
Not resolved	5 (42)	18 (55)	27 (63)	34 (45)	23 (27)		107 (43)
Cause for disease persistence	*n*=5	*n*=18	*n*=27	*n*=34	*n*=23		*n*=107
No treatment	0 (0)	3 (17)	2 (7)	3 (9)	2 (9)		10 (9)
Poor response	2 (40)	5 (28)	5 (19)	9 (26)	8 (35)	0.86	29 (27)
Persistent subretinal fluid	3 (60)	10 (56)	20 (74)	22 (65)	13 (59)		68 (64)
Disease recurrence							
Recurrence	0 (0)	2 (6)	3 (7)	0 (0)	3 (4)	0.22	8 (3)
No recurrence	12 (100)	31 (94)	40 (93)	76 (100)	81 (98)		240 (97)
Subretinal fluid resolution*	*n*=11	*n*=32	*n*=42	*n*=73	*n*=81		*n*=239
Resolved	7 (64)	19 (59)	16 (38)	42 (58)	58 (72)	**0.01**	142 (59)
Not resolved	4 (36)	13 (41)	26 (62)	31 (42)	23 (28)		97 (41)
Time to resolution (months) Mean (median, range)	21 (22, 3-39)	17 (12, 1-62)	18 (10, 0-102)	16 (13, 0-55)	10 (7, 0-45)	0.09	14 (14, 0-143)
Foveal exudation resolution**	*n*=12	*n*=31	*n*=38	*n*=68	*n*=71		*n*=220
Resolved	7 (58)	14 (45)	14 (37)	37 (54)	44 (62)	0.13	116 (53)
Not resolved	5 (41)	17 (55)	24 (63)	31 (46)	27 (38)		104 (47)

Contd...

Table 5: Contd...

Outcomes	1973-1979 *n*=12 eyes in 12 patients (%)	1980-1989 *n*=33 eyes in 33 patients (%)	1990-1999 *n*=43 eyes in 43 patients (%)	2000-2009 *n*=76 eyes in 76 patients (%)	2010-2018 *n*=84 eyes in 84 patients (%)	*P*	Total *n*=248 eyes in 248 patients (%)
Time to resolution (months) Mean (median, range)	21 (18, 9-39)	34 (18, 7-143)	20 (9, 0-121)	19 (16, 0-70)	18 (13.5, 0-45)	0.06	8 (14, 0-143)
Leaking telangiectasia resolution							
Resolved	7 (58)	17 (52)	22 (51)	44 (58)	60 (71)	0.13	150 (60)
Not resolved	5 (41)	16 (48)	21 (49)	32 (42)	24 (29)		98 (40)
Time to resolution (months) Mean (median, range)	21 (22, 2-39)	14 (8, 1-62)	13 (8, 0-102)	22 (16, 0-138)	13 (12, 0-45)	0.17	17 (13, 0-139)
Neovascularization of the iris (NVI)							
Development of NVI	1 (8)	5 (15)	4 (9)	8 (11)	9 (11)	0.94	27 (11)
No development of NVI	11 (92)	28 (85)	39 (91)	68 (89)	75 (89)		221 (89)
Time to development of NVI (months) Mean (median, range)	1 (1, 0-1)	2 (0, 0-21)	43 (22, 0-130)	17 (4, 0-91)	1 (0, 0-2)	**0.04**	11 (0, 0-130)
Tractional retinal detachment (TRD)							
Development of TRD	0 (0)	2 (6)	4 (9)	11 (14)	8 (10)	0.46	25 (10)
No development of TRD	12 (100)	31 (94)	39 (91)	65 (86)	76 (90)		223 (90)
Time to development of TRD (months) Mean (median, range)	NA	11 (11, 8-14)	83 (33, 10-255)	18 (21, 0-98)	13 (11, 3-26)	0.16	26 (12, 0-255)
Glaucoma							
Development of glaucoma	2 (17)	8 (24)	4 (9)	9 (12)	6 (7)	0.12	29 (12)
No development of glaucoma	10 (83)	25 (76)	39 (91)	67 (88)	77 (93)		219 (88)
Time to development of glaucoma Mean (median, range)	2 (2, 0-2)	1 (0, 0-20)	0 (0, 0-0)	2 (2, 0-5)	1 (1, 0-3)	1.00	1 (0, 0-20)
Enucleation							
Enucleation done	2 (17)	9 (27)	6 (14)	10 (13)	5 (6)	**0.04**	32 (13)
Enucleation not done	10 (83)	24 (73)	37 (86)	66 (87)	79 (94)		216 (87)
Time to enucleation (months) Mean (median, range)	0 (0, 0-0)	2 (0, 0-20)	32 (6, 0-170)	34 (7, 0-184)	10 (2, 0-35)	0.54	19 (0, 0-184)
Enucleation by stage	*n*=2	*n*=9	*n*=6	*n*=10	*n*=5		*n*=32
1	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	NA	0 (0)
2	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	NA	0 (0)
3	1 (50)	3 (33)	3 (50)	6 (60)	3 (60)	0.74	16 (50)
4	1 (50)	6 (67)	3 (50)	4 (40)	1 (20)	0.13	15 (47)
5	0 (0)	0 (0)	0 (0)	0 (0)	1 (20)	0.95	1 (3)
Pars plana vitrectomy (PPV)							
PPV done	0 (0)	0 (0)	4 (9)	9 (12)	3 (4)	0.08	16 (6)
PPV not done	12 (100)	35 (100)	39 (91)	67 (88)	81 (96)		232 (94)
Patching							
Patching done	2 (17)	1 (3)	1 (2)	6 (8)	9 (11)	0.27	19 (8)
Patching not done	10 (83)	32 (97)	42 (98)	70 (92)	75 (9)		229 (92)
Outcome of patching	*n*=2	*n*=1	*n*=1	*n*=6	*n*=9		*n*=19
Improvement in vision	1 (50)	1 (100)	0 (0)	1 (17)	3 (33)		6 (32)
Worse vision	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0.47	0 (0)
No change in vision	1 (0)	0 (0)	1 (0)	5 (83)	6 (67)		13 (68)

Bold values indicate significant *P*. *Subretinal fluid present in 239 eyes at date first seen. **Foveal exudation present in 220 eyes at date first seen, NA=Not applicable, Months of follow-up: *Post-hoc* analysis (Bonferroni test) showed that there were significant differences between groups 1 and 4 (*P*=0.04), 1 and 5 (*P*=0.002), 2 and 4 (*P*=0.02), and 2 and 5 (*P*<0.001). There was no significant difference between the means of any other groups (*P*>0.05), Disease resolution: On sub-analysis (Fisher's exact test), disease resolution was more likely in eyes seen from 2010-2018 compared to eyes seen from 1980-1989 (*P*=0.01) and 1990-1999 (*P*=0.002). There were no significant differences in proportion of eyes with disease resolution between other time periods (*P*>0.05). Subretinal fluid resolution: On sub-analysis (Fisher's exact test), subretinal fluid resolution was more likely in eye seen from 2010-2018 compared to eyes seen from 1990-1999 (*P*<0.001). There were no significant differences in proportion of eyes with subretinal fluid resolution between other time periods (*P*>0.05), Enucleation: On sub-analysis (Fisher's exact test), enucleation was less likely in patient seen from 2010-2018 compared to patients seen from 1980-1989 (*P*=0.003). There were no significant differences in proportion of eyes enucleated between other time periods (*P*>0.05)

Switzerland in which mean age at diagnosis was 5 years and they found that younger age at presentation was associated with more advanced stage and worse visual prognosis.[7] There were several features that were more severe in young patients such as the presence of leukocoria, strabismus, areas of peripheral non-perfusion and telangiectasia, and foveal compromise with poor visual acuity and ultimate need for enucleation.[7] In our department, Dalvin *et al*. studied age of onset of Coats disease in 351 cases, the largest-yet studied cohort, and concurred that younger age (≤3 years at diagnosis) typically manifested more advanced Coats disease stage, worse visual acuity, and more likely to require enucleation.[25]

In this analysis of Coats disease, we tabulated treatment strategies by decade of presentation and found important changes over the years, as in the 2010s there was greater use of laser photocoagulation (55% vs. 33% vs. 38% vs. 40% vs. 72%, $P < 0.001$), sub-Tenon corticosteroid (0% vs. 4% vs. 5% vs. 8% vs. 29%, $P < 0.001$), and intravitreal anti-vascular endothelial growth factor (VEGF) (0% vs. 4% vs. 2% vs. 13% vs. 18%, $P = 0.003$), that could have partially lead to less need for enucleation (17% vs. 27% vs. 14% vs. 13% vs. 6%, $P = 0.04$). The use of laser photocoagulation in the past was limited to eyes with nearly flat retina as it was believed that laser to highly detached retina could lead to development of retinal hole and rhegmatogenous detachment. However, several authors have demonstrated that this is not the case and laser treatment can be employed for total retinal detachment, as is often seen in the youngest children.[14,25,26]

There have been few longitudinal studies on Coats disease. Ong *et al*. reviewed 39 cases of Coats disease based on two decades (decade 1 (1995-2005) versus decade 2 (2006-2015).[8] They noted that patients in decade 1 demonstrated more advanced disease and with worse final visual acuity, whereas those from decade 2 were less often managed with observation and had more procedures per eye. In our series over 5 decades, we similarly observed the most advanced disease in the 1980s and gradual shift toward greater treatments with laser photocoagulation, injections of corticosteroid and anti-VEGF with greater resolution of subretinal fluid and fewer cases of enucleation.

There are limitations to this retrospective analysis extending over 5 decades. First, diagnostic accuracy and treatment strategy have improved over time and misdiagnosis as a simulating lesion with eventual diagnostic enucleation is rarely performed nowadays. Further, current improvements in retinal imaging with hand-held portable camera with wide angle fluorescein angiography, ipad tablet ultrasonography, and hand-held optical coherence tomography all add ease and specificity for diagnostic imaging. Most of these imaging modalities were not available or were in rudimentary development during the 1970s and 1980s and were improved in the 1990s. Additionally, improved methods for treatment of total retinal detachment from early macroscopic retinal detachment surgery to current microscopic methods of external drainage, vitrectomy, and periocular or intraocular medication injections have evolved over time. Lasers have improved during this period from relatively immobile xenon arc photocoagulator to more portable argon and diode laser photocoagulation. These factors could have impacted outcomes in this series.

Conclusion

In summary, we have carefully surveyed a single center experience with Coats disease over 5 decades and found no difference in age race, sex, or Coats disease stage at presentation, but did note more advanced exudative retinopathy in the 1980s with need for enucleation, while in the 2010s greater use of laser photocoagulation, injection of medications, and ultimate globe salvage was documented.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Shields JA, Shields CL, Honavar SG, Demirci H, Cater J. Classification and management of coats disease: The 2000 proctor lecture. Am J Ophthalmol 2001;131:572-83.
2. Shields JA, Shields CL, Honavar SG, Demirci H. Clinical variations and complications of coats disease in 150 cases: The 2000 Sanford Gifford memorial lecture. Am J Ophthalmol 2001;131:561-71.
3. Rishi P, Rishi E, Uparkar M, Sharma T, Gopal L, Bhende P, *et al*. Coats' disease: An Indian perspective. Indian J Ophthalmol 2010;58:119-24.
4. Al-Qahtani AA, Almasaud JM, Ghazi NG. Clinical characteristics and treatment outcomes of coats disease in a Saudi Arabian population. Retina 2015;35:2091-9.
5. Cebeci Z, Bayraktar S, Yilmaz YC, Tuncer S, Kır N. Evaluation of follow-up and treatment results in Coats' disease. Turk J Ophthalmol 2016;46:226-31.
6. Daruich AL, Moulin AP, Tran HV, Matet A, Munier FL. Subfoveal nodule in coats disease: Toward an updated classification predicting visual prognosis. Retina 2017;37:1591-8.
7. Daruich A, Matet A, Munier FL. Younger age at presentation in children with Coats disease is associated with more advanced stage and worse visual prognosis: A retirospective study. Retina 2018;38:2239-46.
8. Ong SS, Buckley EG, McCuen BW 2nd, Jaffe GJ, Postel EA, Mahmoud TH, *et al*. Comparison of visual outcomes in Coats' disease: A 20-year experience. Ophthalmology 2017;124:1368-76.
9. Sigler EJ, Randolph JC, Calzada JI, Wilson MW, Haik BG. Current management of coats disease. Surv Ophthalmol 2014;59:30-46.
10. Silodor SW, Augsburger JJ, Shields JA, Tasman W. Natural history and management of advanced Coats' disease. Ophthalmic Surg 1988;19:89-93.
11. Li AS, Capone A Jr, Trese MT, Sears JE, Kychenthal A, De la Huerta I, *et al*. Long-term outcomes of total exudative retinal detachments in stage 3B coats disease. Ophthalmology 2018;125:887-93.
12. Desai SR, Sayem OA, Chakravarti A, Natarajan S. Modified transscleral external drainage of subretinal fluid in high bullous exudative retinal detachment due to Coats' disease. Oman J Ophthalmol 2018;11:181-3.
13. Rao P, Knapp AN, Todorich, Drenser KA, Trese MT, Capone A Jr. Anatomical surgical outcomes of patients with advanced coats disease and coats-like detachments: Review of literature. Novel surgical technique, and subset analysis in patients with facioscapulohumeral muscular dystrophy. Retina 2019; Feb 14. doi: 10.1097/IAE.0000000000002463. [Epub ahead of print]
14. Levinson JD, Hubbard GB. 577-nm yellow laser photocoagulation for Coats disease. Retina 2016;36:1388-94.
15. Ramasubramanian A, Shields CL. Bevacizumab for coats' disease with exudative retinal detachment and risk of vitreoretinal traction. Br J Ophthalmol 2012;96:356-9.

16. Gaillard MC, Mataftsi A, Balmer A, Houghton S, Munier FL. Ranibizumab in the management of advanced coats disease stages 3B and 4: Long-term outcomes. Retina 2014;34:2275-81.
17. Zhang L, Ke Y, Wang W, Shi X, Hei K, Li X. The efficacy of conbercept or ranibizumab intravitreal injection combined with laser therapy for coats' disease. Graefes Arch Clin Exp Ophthalmol 2018;256:1339-46.
18. Belin PJ, Lee AC, Greaves G, Kosoy J, Lieberman RM. The use of bevacizumab in pediatric retinal and choroidal disease: A review. Eur J Ophthalmol 2019; Feb 13:1120672119827773. doi: 10.1177/1120672119827773. [Epub ahead of print].
19. Shields JA, Shields CL. Review: Coats disease: The 2001 LuEsther T. Mertz lecture. Retina 2002;22:80-91.
20. Shields CL, Schoenfeld E, Kocher K, Shukla SY, Kaliki S, Shields JA. Lesions simulating retinoblastoma (pseudoretinoblastoma) in 604 cases. Ophthalmology 2013;120:311-6.
21. Shields JA, Shields CL. Differentiation of Coats' disease and retinoblastoma. J Ped Ophthalmol Strabism 2001;38:262-6.
22. Udyaver S, Dalvin LA, Lim LAS, Mazloumi M, Atalay HT, Khoo CTL, *et al*. Predictors of enucleation in Coats disease: Analysis of 259 eyes at a single center. J AAPOS 2019;[In Press].
23. Khoo CTL, Dalvin LA, Lim LS, Udyaver S, Atalay HT, Mazloumi M, *et al*. Factors predictive of subretinal fluid resolution in Coats disease: Analysis of 177 eyes in 177 patients at a single center. Asia Pac J Ophthalmol 2019; [In Press].
24. Morris B, Foot B, Mulvihill A. A population-based study of coats disease in the United Kingdom I: Epidemiology and clinical features at diagnosis. Eye 2010;24:1797-801.
25. Dalvin LA, Udyaver S, Lim LS, Mazloumi M, Atalay HT, Khoo CTL, *et al*. Coats disease: Clinical features and outcomes by age category in 351 cases. J Pediatr Ophthalmol Strabism 2019; [In Press].
26. Schefler AC, Berrocal AM, Murray TG. Advanced Coats' disease. Management with repetitive aggressive laser ablation therapy. Retina 2008;28:S38-41.