

Uveal Metastasis Based on Patient Sex in 2214 Tumors of 1111 Patients. A Comparison of Female Versus Male Clinical Features and Outcomes

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Background: Lacking in previous studies on uveal metastasis is a robust statistical comparison of patient demographics, tumor features, and overall survival based on patient sex.

Objective: The aim of this study was to evaluate demographics, clinical features, and overall survival of patients with uveal metastasis based on sex.

Method: This is a retrospective analysis. All patients were evaluated on the Ocular Oncology Service, Wills Eye Hospital, PA between January 1, 1974 and June 1, 2017.

Results: A total of 2214 uveal metastases were diagnosed in 1310 eyes of 1111 consecutive patients. A comparison (female versus male) revealed differences across several demographic and clinical features including, among others, mean age at metastasis diagnosis (58 vs 63 years, $P < 0.001$), bilateral disease (21% vs 11%, $P < 0.001$), and mean number of metastases per eye (1.8 vs 1.6 tumors per eye, $P = 0.04$). There were differences in overall mean survival (20 vs 13 months, $P = 0.03$) and 5-year survival (Kaplan-Meier estimate) (31% vs 21%, $P < 0.001$).

Conclusions: There are demographic, clinical, and survival differences when patients with uveal metastases are compared by sex. Understanding these differences can aid the clinician in better anticipating patient outcomes.

Key Words: cancer, choroid, metastasis, sex, uvea

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Ocular metastasis occurs more frequently than primary eye cancer in both females and males.^{1–16} In a series of 420 patients with uveal metastasis from Philadelphia, USA, including 283 females and 137 males, the most common primary cancer sites (in descending order) in females included breast, lung, gastrointestinal tract, cutaneous melanoma, and kidney, whereas the most common sites in males were lung, gastrointestinal tract, prostate, kidney, and cutaneous melanoma.² From Liverpool, England, an analysis of 53 males and 43 females with uveal metastasis revealed that the most common primary cancer sites in females were breast, followed by lung, uterus, and ovary, whereas the primary sites in males were lung, esophagus, prostate, and stomach.³ Additional reports have focused on ocular metastasis to specific uveal tissues or analyzed ocular metastasis from specific primary sites, including breast, lung, and pancreatic cancers, and others.^{4–16}

Lacking in these studies is a robust statistical comparison of patient demographics, tumor features, and overall survival based on patient sex. Herein, we report a large series of patients with uveal metastasis and analyze results based on patient sex, including primary cancer site, clinical features of the tumor, and overall patient survival.

METHODS

Patients with uveal metastasis from the Wills Eye Hospital, Philadelphia, PA, who were evaluated between January 1, 1974, and June 1, 2017, were included. Patients with lymphoproliferative disorders, such as lymphoma, leukemia, and multiple myeloma, were excluded. This analysis adhered to the tenets of the Declaration of Helsinki and was approved by the Institutional Review Board of Wills Eye Hospital.

Data included patient demographics, primary cancer site, uveal metastasis clinical features, tumor management, and survival outcome. Demographic data included patient age at the time of ocular diagnosis, sex, and race. Primary cancer information included site of primary malignancy (breast, lung, kidney, gastrointestinal tract, skin, prostate, thyroid, pancreas, others, unknown), date of primary cancer diagnosis, and interval between primary cancer diagnosis and uveal metastasis. Follow-up interval and overall survival data were collected.

Clinical features included patient symptoms, involved eye (right, left), laterality (unilateral, bilateral), visual acuity, and intraocular pressure. The total number of metastases per eye, anatomic location of the uveal metastases (iris, ciliary body, choroid), tumor basal dimension (millimeter), thickness (millimeter), and color (yellow, orange, brown, other) were recorded.

All tumors were counted; however, if multiple metastatic tumors were present in a single eye, detailed data were recorded for only the largest tumor per uveal tissue (iris, ciliary body, choroid). For iris metastases, presence of hyphema was recorded. For choroidal metastasis, distance to the foveola and optic disc (millimeter), presence of subretinal fluid, and ultrasonographic acoustic quality (dense, hollow) were recorded.

All data were tabulated on Microsoft Excel 2016 and measures of central tendencies (mean, median, range) were obtained using built-in functions. Independent 2-sample *t* test was used to assess statistical significance between continuous data whereas Fisher exact test and chi-square test were used for categorical data. Five-year Kaplan-Meier (KM) survival analysis was performed by grouping censored and death data into half-month intervals. Log-rank test was used to assess statistical significance among KM data and hazard ratios with 95% confidence intervals were calculated. A *P* value <0.05 was considered statistically significant for all tests.

RESULTS

There were a total of 2214 uveal metastases in 1310 eyes of 1111 patients. Demographics and clinical features based on patient sex are listed in Table 1. There were 715 (64%) females and 396 males (36%). A comparison (female vs male) revealed significant difference in mean age at ocular diagnosis (58 vs 63 years, *P* < 0.001), bilateral involvement (21% vs 11%, *P* < 0.001), and mean visual acuity (20/80 vs 20/150, *P* < 0.001). Of the 1111 patients, most were white (88%) with no difference in race distribution between sexes.

The primary cancer site by sex is listed in Table 2. By comparison, uveal metastasis from breast cancer was more common in females (58% vs 1%, *P* < 0.001), whereas metastasis from lung (19% vs 40%, *P* < 0.001), kidney (2% vs 9%, *P* < 0.001), gastrointestinal tract (1% vs 8%, *P* < 0.001), cutaneous melanoma

(1% vs 5%, *P* < 0.001), and prostate cancer (0% vs 6%, *P* < 0.001) was more common in males. Unknown primary cancer site was more common in males (11% vs 21%, *P* < 0.001). The primary cancers classified as other are listed as a footnote in Table 2.

Clinical features of uveal metastasis by sex are listed in Table 3. By comparison, there was no difference per sex in distribution of iris metastasis (7% vs 6%), ciliary body metastasis (2% vs 2%), and choroid metastasis (91% vs 92%). There was significantly more mean number of metastatic tumors per eye in females (1.8 vs 1.6, *P* = 0.04). Regarding choroidal metastasis, there were significant differences in mean tumor base (9.1 vs 10.3 mm, *P* < 0.001), mean tumor thickness (2.8 vs 3.9 mm, *P* < 0.001), yellow color (88% vs 81%, *P* = 0.002), brown color (3% vs 7%, *P* = 0.001), and presence of subretinal fluid (68% vs 79%, *P* < 0.001).

KM survival estimates at 1, 2, 3, 4, and 5 years are listed in Table 4. Considering all uveal metastasis by sex, there were differences in KM survival at 5 years (31% vs 21%, *P* < 0.001) and mean survival (19.8 vs. 12.6 months, *P* = 0.03) (Fig. 1). Regarding specific primary cancer sites per sex, a significant difference in KM survival at 5 years was found with primary lung cancer (24% vs 9%, *P* = 0.04). In the KM analysis, 489 females were censored, compared with 272 males, during the 5-year interval.

Multiple post-hoc analyses were performed. When breast cancer was removed from the female cohort, a comparison of female versus male revealed mean age (60 vs 63 years, *P* = 0.007), bilateral metastases (15% vs 11%, *P* = 0.142), and mean number of tumors per eye (1.7 vs 1.6, *P* = 0.34). When looking only at the female cohort, a comparison of tumor diameter and thickness between breast cancer primary site versus all other primary tumor types revealed a statistically significant difference in tumor thickness (2.4 vs 3.4 mm, *P* < 0.001), but no difference

TABLE 1. Demographics and Clinical Features of Patients

Feature	Patient Sex			Total, n = 1111 Patients
	Female, n = 715 Patients	Male, n = 396 Patients	<i>P</i> Value*	
Age, y, mean (median, range)	58 (59, 10–94)	63 (64, 26–93)	<0.001 [†]	60 (61, 10–94)
Sex, no. (%)				
Male	0 (0)	396 (100)	—	396 (36)
Female	715 (100)	0 (0)	—	715 (64)
Race, no. (%)				
White	631 (89)	351 (89)	0.922	982 (88)
Black	50 (7)	25 (6)	0.710	75 (7)
Asian	11 (1)	5 (1)	0.798	16 (1)
Middle Eastern	1 (<1)	1 (<1)	1.000	2 (1)
Hispanic	8 (1)	4 (1)	1.000	12 (1)
Other	14 (2)	10 (3)	0.526	24 (2)
Eye, no. eyes (%)				
Right	422 (49)	214 (48)	1.000	636 (48)
Left	445 (51)	229 (52)		674 (52)
Laterality, no. (%)				
Unilateral	562 (79)	351 (89)	<0.001	913 (82)
Bilateral	153 (21)	45 (11)		198 (18)
Visual acuity, Snellen mean (median, range), n = 443 male eyes, 887 female eyes	20/80 (20/50, 20/20–NLP)	20/150 (20/60, 20/20–NLP)	<0.001 [†]	20/100 (20/50, 20/20–NLP)

Bold *P* values indicate significant difference.

*Fisher exact test

†Independent sample *t* test.

TABLE 2. Primary Cancer Site

	Patient Sex			Total, n = 1111 Patients
	Female, n = 715 Patients	Male, n = 396 Patients	P Value*	
Primary site, no. (%)				
Breast	413 (58)	3 (1)	<0.001	416 (37)
Lung	135 (19)	160 (40)	<0.001	295 (26)
Kidney	12 (2)	34 (9)	<0.001	46 (4)
GI	10 (1)	30 (8)	<0.001	40 (4)
Cutaneous melanoma	8 (1)	19 (5)	<0.001	27 (2)
Lung carcinoid	17 (2)	7 (2)	0.667	24 (2)
Prostate	0 (0)	23 (6)	<0.001	23 (2)
Thyroid	6 (1)	9 (2)	0.058	15 (1)
Pancreas	6 (1)	2 (1)	0.719	8 (1)
Others [†]	26 (4)	25 (6)	0.051	40 (4)
Unknown	86 (11)	91 (21)	<0.001	177 (15)

GI indicates gastrointestinal. Bold *P* values indicate significant difference.

*Fisher exact test.

[†]Others included: larynx (n = 6), carcinoid (small intestine, appendix, colon, pancreas, testicle) (n = 6), bladder (n = 4), contralateral choroidal melanoma (n = 3), uterus (n = 3), leiomyoma/leiomyosarcoma (n = 3), salivary gland (n = 2), testicle (n = 2), bone (Ewing sarcoma) (n = 2), liver (n = 1), biliary tract (n = 1), scalp (adenocarcinoma) (n = 1), cervix (n = 1), seminal vesicle (n = 1), ovary (n = 1), myxofibrosarcoma (n = 1), trachea (n = 1), and adenoid cystic carcinoma (n = 1).

in tumor diameter (9.3 vs 8.9, $P = 0.28$). For patients with primary lung cancer, tumor diameter was smaller in females compared with that in males (9.2 vs 11.0, $P = 0.005$) whereas tumor thickness was similar (3.4 vs 3.7, $P = 0.25$). When comparing breast cancer versus lung cancer in all patients, subretinal fluid was more common in lung cancer metastasis (67% vs 78%, $P < 0.001$), whereas bilateral disease was more common in breast cancer metastasis (26% vs 14%, $P < 0.001$).

DISCUSSION

Our findings in 1111 patients support what has been reported in 2 other large series on uveal metastasis by Shields et al² (420 patients) and Konstantinidis et al³ (96 patients), in that the most common primary cancer to metastasize to the uvea was breast cancer in females and lung cancer in males. We found additional important details in uveal metastatic disease per sex. We note that the mean age at diagnosis of uveal metastasis in females (58 years) was significantly younger than in males (63 years) ($P < 0.001$). This age difference was likely because of the predominance of breast cancer in females (58% of uveal metastasis in females) and lung cancer in males (40% of uveal metastasis in males), given that the mean age at breast cancer diagnosis in the United States is 61 years, somewhat lower than the mean age at lung cancer diagnosis of 70 years.¹ Shields et al² reported an average age of 58 years at time of uveal metastasis for all patients, most likely driven by the large cohort of females with breast cancer metastasis (47% of patients) in that study. In a series of 264 cases of uveal metastasis¹² from breast cancer specifically, the average age at diagnosis was 56 years (median 57, range 23–84), slightly younger than the female cohort in our study. In a series of 194 patients with uveal metastasis¹³ from lung cancer specifically, the mean age at diagnosis was 62 years (55% male), slightly younger than the average age of men in our study. When patients with primary breast cancer were removed from the female cohort in our study, the mean age at uveal metastasis diagnosis in females increased from 58 to 60 years, but continued to demonstrate significant difference when compared with males (63 years) ($P = 0.007$). This suggests that other factors, apart from the

predominance of breast cancer in females and the related younger age of onset, might be responsible for the age difference between females and males with uveal metastasis.

By comparison (female vs male), we found a relatively lower number of metastasis from lung (19% vs 40%), kidney (2% vs 9%), gastrointestinal (1% vs 8%), and cutaneous melanoma (1% vs 5%) malignancies in females. According to the US Centers for Disease Control and Prevention,¹ the 2014 incidence rates (per 100,000) of these primary cancers in females versus males revealed lung (50.8 vs 68.1), kidney (11.3 vs 22.0), colorectal (33.7 vs 44.0), and cutaneous melanoma (16.9 vs 27.6).¹ The lower incidence rates of these cancers in females correlate with the fewer related uveal metastasis. The lower percentage of brown choroidal metastases in females was likely because of the lower percentage of cutaneous melanoma metastasis in females.

Previous reports have revealed the bilateral and multifocal nature of uveal metastasis from breast cancer compared with other primary cancer types.^{2,3,12,13} The high rate of uveal metastasis from breast cancer in females likely contributed to the increased proportion of bilateral uveal metastasis and increased number of tumors per eye in females in this study. In other reports, bilateral uveal metastasis from breast cancer has ranged between 18% and 33% of patients, whereas bilateral uveal metastasis owing to lung cancer was less common, ranging from 14% to 20%.^{2,3,11,12} Our data showed that 26% of patients with uveal metastasis from breast cancer demonstrated bilateral involvement compared with 14% of patients with metastasis from lung cancer ($P < 0.001$). When we removed breast cancer patients from the female cohort, the percentage of bilateral uveal metastasis in females was reduced to 15%, still higher than in males (11%), but without significance ($P = 0.14$). Similarly, when breast cancer was removed from the female cohort, the mean number of tumors per eye in females decreased from 1.8 to 1.7 and failed to demonstrate significance when compared with a mean of 1.6 tumors per eye in males ($P = 0.34$). These analyses support previous suggestions regarding the particular bilateral and multifocal nature of uveal metastasis from breast cancer.^{2,3,12,13}

TABLE 3. Metastasis Features

Tumor Feature for Largest Uveal Metastasis	Patient Sex			Total, n = 1342 Tumors
	Female, n = 890 Tumors	Male, n = 452 Tumors	P Value*	
Tumor location, no. (%)			0.335 [†]	
Iris	61 (7)	40 (6)		101 (8)
Ciliary body	17 (2)	11 (2)		28 (2)
Choroid	812 (91)	401 (92)		1213 (90)
Number of tumors per eye, mean (median, range)	1.8 (1, 1–29)	1.6 (1, 1–13)	0.036 [‡]	1.7 [1, 1–29]
Iris metastasis (largest tumor) (n = 101 tumors)				
Base, mean, mm	6.4	6.9	0.541 [‡]	6.6
Thickness, mean, mm	2.7	2.5	0.567 [‡]	2.6
Color, no. (%)				
Yellow	35 (58)	19 (48)	0.415	54 (54)
Orange	3 (5)	6 (15)	0.150	9 (9)
Brown	4 (7)	5 (13)	0.477	9 (9)
Other	17 (30)	10 (25)	0.657	27 (27)
Hyphema, no. (%)				
Yes	8 (13)	9 (23)	0.279	17 (17)
No	52 (92)	31 (72)		83 (84)
Ciliary body metastasis (largest tumor) (n = 28 tumors)				
Base, mean, mm	10.4	13.3	0.297 [‡]	11.6
Thickness, mean, mm	4.6	6.3	0.252 [‡]	5.3
Color, no. (%)				
Yellow	9 (56)	6 (55)	1.000	15 (56)
Orange	1 (6)	2 (18)	0.543	3 (11)
Brown	3 (19)	0 (0)	0.258	3 (11)
Other	3 (19)	3 (27)	0.653	6 (22)
Choroidal metastasis (largest tumor) (n = 1213 tumors)				
Base, mean, mm	9.1	10.3	<0.001 [‡]	9.5
Thickness, mean, mm	2.8	3.9	<0.001 [‡]	3.2
Foveola, mean, mm	2.2	2.1	0.680 [‡]	2.1
Optic disc, mean, mm	2.6	2.2	0.033 [‡]	2.5
Color, no. (%)				
Yellow	717 (88)	326 (81)	0.002	1043 (86)
Orange	59 (7)	37 (9)	0.258	96 (8)
Brown	22 (3)	28 (7)	0.001	50 (4)
Other	14 (2)	10 (2)	0.385	24 (2)
Subretinal fluid, no. (%)				
Yes	555 (68)	315 (79)	<0.001	870 (72)
No	257 (31)	86 (20)		343 (28)
Ultrasound density				
Dense, %	81	77	0.154	80
Hollow, %	19	23		20

Bold *P* values indicate significant difference.

*Fisher exact test.

†Chi-square test.

‡Independent sample *t* test.

Females demonstrated smaller choroidal metastases in base (9.1 vs 10.3 mm, $P < 0.001$) and thickness (2.8 vs 3.9 mm, $P < 0.001$) compared with males. A previous report documented a tendency toward thinner tumors in metastatic breast cancer (mean 2 mm thickness), compared to lung (3 mm), gastrointestinal (4 mm), kidney (4 mm), prostate (3 mm), and unknown (3 mm).² In the current analysis, we compared females with choroidal metastasis from breast cancer to females with metastasis from all other primary sites and found no significant difference in tumor basal diameter (9.3 vs 8.9, $P = 0.28$), but noted that tumor thickness was significantly less in those females with breast metastasis (vs others) (2.4 vs 3.4 mm, $P < 0.001$). The overall difference in choroidal metastasis thickness (thinner in females) was possibly because of the flatter nature of choroidal metastases from breast cancer and the high proportion of breast cancer in the

female cohort. When comparing females and males with choroidal metastasis from lung cancer, there was no significant difference in tumor thickness (3.4 vs 3.7, $P = 0.25$); however, tumor basal diameter was significantly smaller in females (9.2 vs 11.0, $P = 0.005$). The overall difference in choroidal metastasis basal diameter (larger in males) is possibly explained by the high proportion of lung cancer in the male cohort.

The smaller tumor size in females (base and thickness) could be responsible for the fewer number of tumors associated with subretinal fluid in females (68% vs 78%, $P < 0.001$). However, when comparing all patients with breast cancer metastases to all patients with lung cancer metastases, subretinal fluid was far more common with lung cancer metastases (67% in breast vs 78% in lung, $P < 0.001$). This is possibly explained by the larger tumor base of metastasis from lung cancer or the possibility that

TABLE 4. Kaplan–Meier Survival Analysis and Mean Survival

Primary Site	Kaplan-Meier Survival Analysis						Mean Survival, Mo (Median, Range)		
	1 y	2 y	3 y	4 y	5 y	Comparison of Female Vs Male		P Value [†]	
						P value*	Hazard Ratio for Death (95% CI)		
Total									
Female (n = 715 pts, 489 censored)	0.664	0.514	0.393	0.355	0.305	<0.001	0.6 (0.5–0.8)	19.8 (9.8, 0.3–209)	0.030
Male (n = 396 pts, 272 censored)	0.473	0.317	0.265	0.246	0.205			12.6 (5.7, 0.3–155)	
Breast									
Female (n = 413 pts, 265 censored)	0.684	0.523	0.378	0.347	0.275	0.935	1.1 (0.2–7.2)	22.2 (11.0, 0.4–209)	0.970
Male (n = 3 pts, 2 censored)	1.000	0	0	0	0			23.9 (23.9, 23.9–23.9)	
Lung									
Female (n = 135 pts, 99 censored)	0.582	0.391	0.298	0.238	0.238	0.009	0.6 (0.4–0.9)	11.9 (6.7, 0.3–68.9)	0.978
Male (n = 160 patients, 108 censored)	0.370	0.222	0.178	0.133	0.089			11.3 (5.2, 0.3–111)	
Kidney									
Female (n = 12 pts, 9 censored)	0	0	0	0	0	0.174	2.6 (0.4–15)	6.4 (6.3, 1.6–11.3)	0.404
Male (n = 34 pts, 29 censored)	0.675	0.338	0	0	0			9.9 (9.8, 2.9–19.6)	
Gastrointestinal									
Female (n = 10 pts, 5 censored)	0.714	0.357	0.357	0.357	0.357	0.129	0.4 (0.2–1.1)	23.3 (12.4, 1.8–85.1)	0.209
Male (n = 30 pts, 15 censored)	0.218	0.109	0.109	0.109	0.109			8.8 (3.9, 1.0–63.9)	
Cutaneous melanoma									
Female (n = 8 pts, 5 censored)	0.800	0.800	0.533	0.533	0.533	0.273	0.4 (0.1–1.8)	18.5 (18.5, 8.4–28.7)	0.227
Male (n = 19 pts, 14 censored)	0.686	0	0	0	0			8.5 (5.7, 2.3–16.9)	
Lung carcinoid									
Female (n = 17 pts, 15 censored)	0.900	0.900	0.900	0.900	0.900	0.527	NE	34.9 (34.9, 8.6–61.1)	0.540
Male (n = 7 pts, 6 censored)	1.000	1.000	1.000	1.000	1.000			106 (106, 106–106)	
Prostate									
Female (n = 0 pts)	NA	NA	NA	NA	NA	NE	NE	NE	NE
Male (n = 23 pts, 17 censored)	0.544	0.363	0.363	0.363	0.363			32.2 (8.5, 0.5–155)	
Thyroid									
Female (n = 6 pts, 2 censored)	0.250	0.250	0.250	0.250	0.250	0.823	0.85 (0.2–3.5)	9.1 (10.5, 5.0–11.7)	0.726
Male (n = 9 pts, 4 censored)	0.486	0.243	0	0	0			11.6 (11.6, 1.8–29.8)	
Pancreas									
Female (n = 6 pts, 4 censored)	0	0	0	0	0	NE	NE	3.9 (3.9, 3.1–4.7)	0.504
Male (n = 2 pts, 1 censored)	0	0	0	0	0			4.8 (4.8, 4.8–4.8)	
Others [‡]									
Female (n = 22 pts, 16 censored)	0.593	0.593	0.593	0.593	0.593	0.856	1.1 (0.3–4.2)	10.1 (4.9, 1.7–42.4)	0.649
Male (n = 18 pts, 14 censored)	0.698	0	0	0	0			7.1 (7.4, 0.9–16.7)	
Unknown primary									
Female (n = 86 pts, 69 censored)	0.726	0.558	0.489	0.391	0.391	0.095	0.6 (0.3–1.1)	25.4 (10.2, 0.4–106)	0.195
Male (n = 91 pts, 62 censored)	0.462	0.391	0.342	0.342	0.285			11.8 (5.0, 0.3–87.7)	

CI indicates confidence interval; NA, not applicable; NE, not estimable; pts, patients; Vs, versus. Bold P values and hazard ratio values indicate significant difference.

*Log-rank test.

†Independent sample t test.

‡Others included: larynx (n = 6), carcinoid (small intestine, appendix, colon, pancreas, testicle) (n = 6), bladder (n = 4), contralateral choroidal melanoma (n = 3), uterus (n = 3), leiomyoma/leiomyosarcoma (n = 3), salivary gland (n = 2), testicle (n = 2), bone (Ewing sarcoma) (n = 2), liver (n = 1), biliary tract (n = 1), scalp (adenocarcinoma) (n = 1), cervix (n = 1), seminal vesicle (n = 1), ovary (n = 1), myxofibrosarcoma (n = 1), trachea (n = 1), and adenoid cystic carcinoma (n = 1).

choroidal metastases from different primary sites display different exudative profiles. Other sex-related differences, such as better mean visual acuity in females, could be multifactorial with smaller tumor size, less frequent subretinal fluid, and younger age contributing. There was no sex difference in the precise distances of choroidal metastasis from the visually vital optic disc and foveola.

Relatively few studies have addressed overall survival for patients with uveal metastasis.^{2–5,11–13} Freedman and Folk⁴ reported that patients with metastasis to the eye and orbit from breast cancer (55 patients) lived longer (mean survival time = 22 months) than those with metastasis owing to lung cancer (16 patients) (mean survival time = 6 months). A recent comprehensive analysis from our department on prognosis of uveal metastasis based on primary cancer site (1111 patients) revealed 1-year and 5-year KM survival estimates of 57% and 24% for all primary cancer sites. In that analysis, patients with uveal metastasis from breast cancer versus lung cancer had 5-year KM survival estimates of 25%

versus 13%, with a statistically significant difference. In a report specifically regarding breast cancer metastasis to the uvea, 1-year and 5-year KM survival estimates of 65% and 24%, respectively, were reported.¹² With specific investigation of lung cancer with uveal metastasis, survival at 1-year was 45% and there was no information on 5-year survival.¹³ In this analysis of 1111 patients with uveal metastasis based on sex, we note that overall 1-year and 5-year KM survival for females (66% and 31%, respectively) and males (47% and 21%, respectively) resemble those listed above, specifically for breast and lung cancer.^{12,13} It is likely that the predominance of uveal metastasis from breast cancer in females and the predominance of lung cancer in males are responsible for the overall survival differences per sex; however, other factors, like patient age, tumor size, and malignant potential of each specific tumor type, could be contributory. In particular, when focusing on survival after uveal metastasis from lung cancer by sex, 5-year survival in females (24%) was significantly longer than males (9%). This could be because of younger age of females with lung

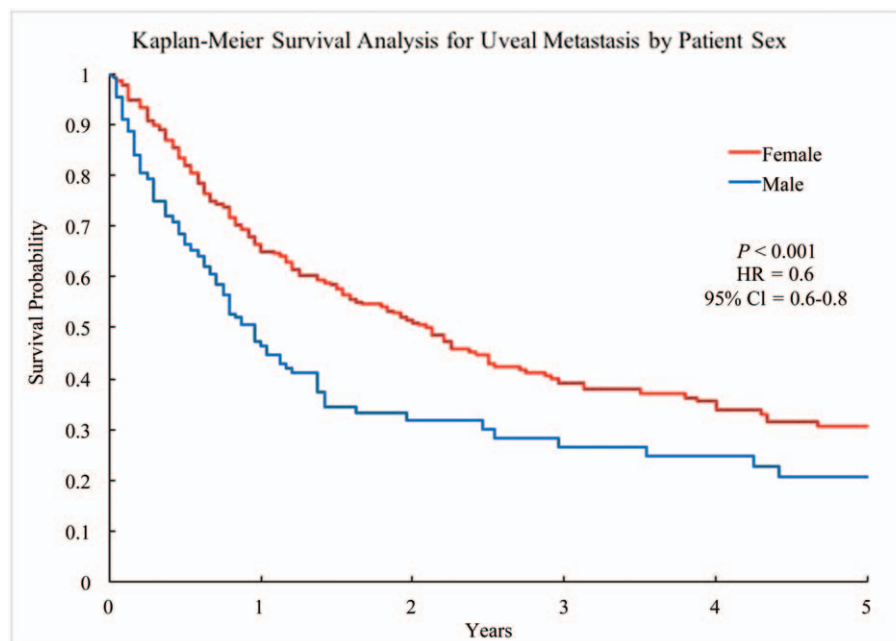


FIGURE 1. Kaplan-Meier survival analysis for patients with uveal metastasis based on sex. CI indicates confidence interval; HR, hazard ratio for death (female/male).

metastasis compared with males (61 years vs 64 years, $P = 0.04$), tumor size, and other factors.

This is a large series encompassing a broad time period and the survival data reported herein are possibly limited by the broad grouping of survival outcomes. Given that survival for some patients with metastatic cancer has increased in recent years, a study addressing survival trends of patients with uveal metastasis through the decades could be of interest.¹⁷

In conclusion, over a 43-year span at a major ocular oncology center, uveal metastasis was more common in females (64%) than males (36%). Females most commonly presented with metastasis from breast cancer (58%), whereas males most commonly demonstrated underlying lung cancer (40%). Females presented at a younger age, with better visual acuity, more bilateral metastases, smaller tumor size, and less frequent association with subretinal fluid, compared with males. After detection and management of uveal metastasis, overall survival was significantly better in females compared with males. Understanding sex differences in uveal metastasis can provide better understanding in patient care.

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