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 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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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 | Female, n = 715 Patients | Male, n = 396 Patients | P Value | Total, n = 1111 Patients |
|---------|--------------------------|------------------------|---------|--------------------------|
| 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) | 1.000 | 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) |

| Table 2. Uveal Metastasis By Sex |
|-------------------------|-------------------------|-------------------------|
| Feature | Female, n = 715 Patients | Male, n = 396 Patients | P Value | Total, n = 1111 Patients |
| Primary cancer site | | | | |
| Breast | 714 (99) | 395 (100) | — | 1109 (100) |
| Lung | 40 (6) | 24 (6) | 0.814 | 64 (6) |
| Kidney | 4 (1) | 2 (0.5) | 0.402 | 6 (0.5) |
| Gastrointestinal tract | 3 (0.4) | 2 (0.5) | 0.798 | 5 (0.5) |
| Cutaneous melanoma | 2 (0.3) | 2 (0.5) | 0.600 | 4 (0.4) |
| Prostate | 0 (0) | 6 (1) | 0.007 | 6 (1) |
| Other | 1 (0.1) | 2 (0.5) | 0.550 | 3 (0.3) |

| Table 3. Laterality and Bilateral Involvement |
|-------------------------|-------------------------|-------------------------|
| Laterality, no. (%) | Female, n = 715 Patients | Male, n = 396 Patients | P Value | Total, n = 1111 Patients |
| Unilateral | 562 (79) | 351 (89) | <0.001 | 913 (82) |
| Bilateral | 153 (21) | 45 (11) | 198 (18) | |

| Table 4. Visual Acuity |
|-------------------------|-------------------------|-------------------------|
| 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) |

| Table 5. Race Distribution Between Sexes |
|-------------------------|-------------------------|-------------------------|
| Race, no. (%) | Female, n = 715 Patients | Male, n = 396 Patients | P Value | Total, n = 1111 Patients |
| 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) |

**Bold** P values indicate significant difference.

†Fisher exact test

\( t \) test.
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 al\(^6\) (420 patients) and Konstantinidis et al\(^9\) (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. Shields et al\(^5\) 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 metastasis\(^5\) 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 metastasis\(^5\) 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).\(^2\) 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.\(^2,3,12,13\)

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**TABLE 2. Primary Cancer Site**

| Cancer Site          | Female, n = 715 Patients | Male, n = 396 Patients | \(P\) Value* | Total, n = 1111 Patients |
|----------------------|--------------------------|------------------------|--------------|--------------------------|
| **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 carcinoma       | 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\(^1\)         | 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.

\(^1\)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 (\(n = 1\)).
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 3. Metastasis Features**

| Tumor Feature for Largest Uveal Metastasis | Patient Sex | Female, \(n = 890\) Tumors | Male, \(n = 452\) Tumors | \(P\) Value\(^a\) | Total, \(n = 1342\) Tumors |
|------------------------------------------|-------------|-----------------------------|--------------------------|-------------------|---------------------|
| Tumor location, no. (%) | Iris | 61 (7) | 40 (6) | 0.335\(^b\) | 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) | \(0.036^a\) | 1.7 [1, 1–29] |
| Iris metastasis (largest tumor) (\(n = 101\) tumors) | Base, mean, mm | 6.4 | 6.9 | 0.541\(^b\) | 6.6 |
| Thickness, mean, mm | 2.7 | 2.5 | 0.567\(^b\) | 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\(^b\) | 11.6 |
| Thickness, mean, mm | 4.6 | 6.3 | 0.252\(^b\) | 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 | \(<0.001^a\) | 9.5 |
| Thickness, mean, mm | 2.8 | 3.9 | \(<0.001^a\) | 3.2 |
| Foveola, mean, mm | 2.2 | 2.1 | 0.680\(^b\) | 2.1 |
| Optic disc, mean, mm | 2.6 | 2.2 | 0.033\(^b\) | 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.

\(^a\)Chi-square test.

\(^b\)Independent sample \(t\) test.

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chondrometastases 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 fovea.

Relatively few studies have addressed overall survival for patients with uveal metastasis. Freedman and Folk 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. With specific investigation of lung cancer with uveal metastasis, survival at 1-year was 45% and there was no information on 5-year survival. In this analysis of 1111 patients, survival at 1-year was 45% and there was no information on 5-year survival. In this analysis of 1111 patients, survival at 1-year was 45% and there was no information on 5-year survival. In this analysis of 1111 patients, survival at 1-year was 45% and there was no information on 5-year survival. In this analysis of 1111 patients, survival at 1-year was 45% and there was no information on 5-year survival. In this analysis of 1111 patients, survival at 1-year was 45% and there was no information on 5-year survival.

| Primary Site | 1 y | 2 y | 3 y | 4 y | 5 y | P value | Hazard Ratio for Death (95% CI) | P Value |
|-------------|-----|-----|-----|-----|-----|---------|---------------------------------|---------|
| Breast | 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 | 0.473 | 0.317 | 0.265 | 0.246 | 0.205 | 0.740 | 0.4 (0.3–0.5) | 12.6 (5.7, 0.3–155) | 0.030 |
| Lung | 0.658 | 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 |
| Female | 1.000 | 0 | 0 | 0 | 0 | 0.00 | 0.4 (0.1–1.8) | 23.9 (23.9, 23.9–23.9) | 0.970 |
| Male | 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 |
| Kidney | 0.370 | 0.222 | 0.178 | 0.133 | 0.089 | 0.174 | 2.6 (0.1–5.1) | 11.3 (5.2, 0.3–111) | 0.480 |
| Female | 0 | 0 | 0 | 0 | 0 | 0.174 | 2.6 (0.1–5.1) | 6.4 (6.3, 1.6–11.3) | 0.480 |
| Male | 0.675 | 0.338 | 0 | 0 | 0 | 0.174 | 2.6 (0.1–5.1) | 9.9 (9.8, 2.3–19.6) | 0.480 |
| Gastrointestinal | 0.714 | 0.357 | 0.357 | 0.357 | 0.357 | 0.129 | 0.4 (0.2–1.1) | 23.3 (12.4, 1.8–115) | 0.209 |
| Female | 0.686 | 0.409 | 0.349 | 0.298 | 0.298 | 0.237 | 0.4 (0.1–1.8) | 18.5 (18.5, 8.4–29.7) | 0.227 |
| Male | 0.800 | 0.503 | 0.533 | 0.533 | 0.533 | 0.237 | 0.4 (0.1–1.8) | 8.5 (5.7, 2.7–16.9) | 0.227 |
| Lung carcinoma | 0.900 | 0.900 | 0.900 | 0.900 | 0.900 | 0.527 | NE | 34.9 (34.9, 8.6–61.1) | 0.540 |
| Female | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 0.527 | NE | 106 (106, 106–106) | NE |
| Male | 0.544 | 0.363 | 0.363 | 0.363 | 0.363 | 0.174 | 2.6 (0.1–5.1) | 32.2 (8.5, 0.5–155) | NE |
| Prostate | NA | NA | NA | NA | NA | NE | NE | NE | NE |
| Male | 0.548 | 0.363 | 0.363 | 0.363 | 0.363 | 0.174 | 2.6 (0.1–5.1) | 9.1 (10.5, 5.0–21.7) | 0.726 |
| Thyroid | 0.250 | 0.250 | 0.250 | 0.250 | 0.250 | 0.823 | 0.8 (0.2–3.5) | 116 (11.6, 1.8–29.8) | 0.726 |
| Female | 0.486 | 0.243 | 0 | 0 | 0 | 0.823 | 0.8 (0.2–3.5) | 9.1 (10.5, 5.0–21.7) | 0.726 |
| Pancreas | 0 | 0 | 0 | 0 | 0 | NE | NE | NE | NE |
| Female | 0 | 0 | 0 | 0 | 0 | 0.823 | 0.8 (0.2–3.5) | 9.1 (10.5, 5.0–21.7) | 0.726 |
| Male | 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 |
| Others | 0.698 | 0 | 0 | 0 | 0 | 0.823 | 0.8 (0.2–3.5) | 7.1 (7.4, 0.9–16.7) | 0.649 |
| Female | 0.393 | 0.393 | 0.393 | 0.393 | 0.393 | 0.823 | 0.8 (0.2–3.5) | 25.4 (10.2, 0.4–106) | 0.195 |
| Male | 0.462 | 0.391 | 0.342 | 0.285 | 0.285 | 0.823 | 0.8 (0.2–3.5) | 11.8 (5.0, 0.3–87.7) | 0.195 |

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), contratralateral 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).
Uveal 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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REFERENCES

1. U.S. Cancer Statistics Working Group. United States Cancer Statistics: 1999-2014 Incidence and Mortality Web-based Report. Atlanta: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention and National Cancer Institute; 2017. Available at: www.cdc.gov/uscs.

2. Shields CL, Shields JA, Gross NE, et al. Survey of 520 eyes with uveal metastases. Ophthalmology. 1997;104:1265–1276.

3. Konstantinidis I, Rospond-Kubik I, Zeolite I, et al. Management of patients with uveal metastases at the Liverpool Ocular Oncology Centre. Br J Ophthalmol. 2014;98:92–98.

4. Freedman M, Folk JC. Metastatic tumors to the eye and orbit patient survival and clinical characteristics. Arch Ophthalmol. 1987;105:1215–1219.

5. Shields CL, Welch RJ, Malik K, et al. Uveal metastasis: Clinical features and survival outcome of 2214 tumors in 1111 patients based on primary tumor origin. Mid East Afr J Ophthalmol. 2018;25:81–90.

6. Ferry AP, Font RL. Carcinoma metastatic to the eye and orbit. A clinicopathologic study of 227 cases. Arch Ophthalmol. 1974;92:276–286.

7. Stephens RF, Shields JA. Diagnosis and management of cancer metastatic to the uvea. A study of 70 cases. Ophthalmology. 1978;86:1336–1349.

8. Shields JA, Shields CL, Kirati H, et al. Metastatic tumors to the iris in 40 patients. Am J Ophthalmol. 1995;119:422–430.

9. Shields CL, Kaliki S, Crabtree GS, et al. Iris metastasis from systemic cancer in 104 patients: The 2014 Jerry A. Shields Lecture. Cornea. 2015;34:42–48.

10. Arepalli S, Kaliki S, Shields CL. Choroidal metastases: origin, features,1; and therapy. Indian J Ophthalmol. 2015;63:122–127.

11. Shields JA, Shields CL. Intraocular Tumors. An Atlas and Textbook. 3rd ed, Philadelphia: Lippincott Wolters Kluwers; 2016, 213–245.

12. Demirci H, Shields CL, Chao AN, et al. Uveal metastasis from breast cancer in 264 patients. Am J Ophthalmol. 2003;136:264–271.

13. Shah SU, Mashayekhi A, Shields CL, et al. Uveal metastasis from lung cancer: clinical features, treatment, and outcome in 194 patients. Ophthalmology. 2014;121:252–257.

14. Shah SU, Shields CL, Biancotto CG, et al. Pancreatic cancer metastasis to choroid. Ophthalmology. 2011;118:1483.

15. de Bustros S, Augsburger JJ, Shields JA, et al. Intraocular metastases from cutaneous malignant melanoma. Arch Ophthalmol. 1985;103:937–940.

16. Harbour JW, De Potter P, Shields CL, et al. Uveal metastasis from carcinoid tumor. Clinical observations in nine cases. Ophthalmology. 1994;101:1084–1090.

17. Gobbin E, Ezzalfani M, Dieras V, et al. Time trends of overall survival among metastatic breast cancer patient in the real-life ESME cohort. Eur J Cancer. 2018;96:17–24.