

# Uveal and conjunctival melanomas: disease course and outcomes in Chinese patients

Julia YY Chan \*, Stacey Carolyn Lam, Hunter KL Yuen

## ABSTRACT

**Introduction:** Epidemiological studies of ocular melanomas have largely focused on Caucasian populations. This study reviewed the course and outcomes of uveal melanoma (UM) and conjunctival melanoma (CM) in Chinese patients.

**Methods:** This retrospective study included patients with UM and CM who received treatment in a tertiary eye centre in Hong Kong from January 1994 to December 2019. Data were recorded concerning patient demographics, tumour laterality, tumour characteristics, investigations performed, treatment regimen, and final outcomes.

**Results:** During the 25-year study period, there were 13 patients with UM and 11 patients with CM who did not display nodal or systemic involvement at diagnosis. The mean  $\pm$  standard deviation ages at diagnosis of UM and CM were  $59 \pm 15.8$  and  $57 \pm 13.9$  years, respectively. There were more men among patients with UM than among those with CM ( $P=0.042$ ). Most patients with UM underwent primary enucleation ( $n=12$ ; 92.3%), whereas most patients with CM underwent orbital exenteration

( $n=9$ ; 81.8%). The prognosis was significantly worse for CM than for UM. The median disease-free survival were 5.2 years (range, 0.7-20.5) and 2.1 years (range, 0.1-24.9) for UM and CM, respectively. Melanoma-related mortality was significantly higher among patients with CM than among those with UM ( $P=0.006$ ).

**Conclusion:** Compared with UM, CM has higher rates of systemic metastasis and tumour-related mortality in Hong Kong Chinese patients, regardless of prior definitive treatment.

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<sup>1,2</sup> **JYY Chan \***, FCOphthHK, FHKAM (Ophthalmology)

<sup>1,2</sup> **SC Lam**, FCOphthHK, FHKAM (Ophthalmology)

<sup>1,2</sup> **HKL Yuen**, FRCOphth, FRCSEd

<sup>1</sup> Hong Kong Eye Hospital, Hong Kong SAR, China

<sup>2</sup> Department of Ophthalmology and Visual Sciences, The Chinese University of Hong Kong, Hong Kong SAR, China

\* Corresponding author: yy.chan@link.cuhk.edu.hk

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### New knowledge added by this study

- Among Chinese patients, conjunctival melanoma constituted a larger proportion of ocular melanoma cases than previously identified in Caucasian populations, similar to the findings in a Korean study.
- Compared with uveal melanoma, conjunctival melanoma has a worse prognosis with a higher rate of metastasis, shorter disease-free survival, and shorter overall survival.

### Implications for clinical practice or policy

- Primary enucleation is an effective treatment for patients with uveal melanoma, but patients with conjunctival melanoma may experience systemic metastasis despite radical treatment with wide excisional biopsy or primary orbital exenteration.
- Ophthalmologists and oncologists should offer long-term follow-up with regular systemic surveillance to patients with conjunctival melanoma who have received definitive treatment.

## Introduction

Primary ocular melanoma from melanocytes within the eye constitutes uveal melanoma (UM), whereas ocular melanoma from melanocytes on the globe surface is considered conjunctival melanoma (CM). Although both UM and CM develop from similar neural crest lineages and are classified as ocular melanomas, they have distinct clinical behaviours, management, prognosis, cancer staging features, and molecular characteristics. Overall, 85% of melanomas in ocular regions arise from the uvea (iris, choroidal, and ciliary body), 5% arise from the conjunctiva, and 10% occur in other sites.<sup>1</sup> The most

common site of UM is the choroid, which is involved in 90% of cases.<sup>2</sup>

For most cases of UM, the primary treatment is enucleation. Alternative options include plaque brachytherapy and proton beam radiation; these options are currently unavailable in Hong Kong and similar Asian countries (eg, Singapore). Systemic metastases of UM most commonly affect the liver, followed by lung and bone. Conjunctival melanoma is usually managed by complete excisional biopsy with wide surgical margins, using a ‘no-touch’ technique. Adjuvant therapies such as cryotherapy or topical mitomycin C are offered, followed by

reconstruction with an amniotic membrane graft. Orbital exenteration may be necessary for advanced tumours where local resection is not feasible. Metastatic disease, often to regional lymph nodes and the brain, occurs in 20% to 30% of patients with CM.<sup>3</sup>

Melanomas are generally rare tumours and their incidences are particularly low in Asian populations. The annual incidence of UM in Caucasian populations is 5.1 cases per million,<sup>2</sup> whereas the respective incidences in Japanese<sup>4</sup> and Korean<sup>5</sup> populations are 0.2 and 0.6 cases per million. The incidences of CM are similar: 0.2 to 0.5 cases per million in Caucasian populations<sup>3</sup> and 0.15 cases per million in Asian populations.<sup>6</sup> Because of this rarity among Asian populations, very few studies have focused on Chinese patients. Epidemiological studies have largely involved Caucasian populations. Clinical characteristics may differ in Asian populations; for example, Asian patients are initially diagnosed with UM<sup>5</sup> and CM<sup>6</sup> at younger ages.

Known risk factors for UM include fair skin, light-coloured eyes, congenital ocular melanocytosis, ocular melanocytoma, and *BAP1* tumour predisposition syndrome.<sup>7</sup> In contrast, risk factors for CM include increased conjunctival pigmentation and a history of primary acquired melanosis. Predictors of recurrence or new tumour formation after CM treatment are older age, a history of prior conjunctival surgery, and advanced T subclassification in the American Joint Committee on Cancer (AJCC) staging system.<sup>8</sup>

This study explored the disease course and outcomes of UM and CM in Chinese patients without nodal metastasis on presentation.

## Methods

This retrospective study included patients who received treatment for UM or CM in a single tertiary ophthalmic centre in Hong Kong between January 1994 and December 2019. Inclusion criteria included Chinese ethnicity and imaging-confirmed lack of tumour dissemination at diagnosis. Exclusion criteria were <6 months of follow-up, insufficient available information, loss to follow-up, or presence of any precursor lesions (eg, atypical primary acquired melanosis). The following data were recorded: patient demographics, tumour laterality, tumour characteristics (eg, presentation and staging according to the AJCC Cancer Staging Manual [8th Edition]<sup>9,10</sup>), investigations performed, treatment regimen, and final outcomes. The study adhered to the principles outlined in the Declaration of Helsinki.

Provisional clinical diagnoses of UM and CM were made based on each patient's medical history, primary acquired melanosis status, and clinical presentation. Final diagnoses of UM and

## 葡萄膜黑色素瘤與結膜黑色素瘤：華裔患者的疾病歷程及結果

陳欣遇、林懿德、袁國禮

**簡介：**眼部黑色素瘤的流行病學研究一直集中在白人。本研究回顧葡萄膜黑色素瘤與結膜黑色素瘤的華裔患者的疾病歷程及結果。

**方法：**本回顧性研究的對象是於1994年1月至2019年12月期間在香港一間三級眼科中心接受治療的葡萄膜黑色素瘤與結膜黑色素瘤患者，紀錄的數據包括患者的人口統計資料、腫瘤方位、腫瘤特徵、所進行的調查、治療方案及最終結果。

**結果：**在為期25年的研究中，共有13名葡萄膜黑色素瘤患者及11名結膜黑色素瘤患者在診斷時未有顯示牽涉淋巴結或出現器官轉移。確診葡萄膜黑色素瘤及結膜黑色素瘤的年齡中位數 ± 標準差分別為 59 ± 15.8及57 ± 13.9歲。與結膜黑色素瘤相比，葡萄膜黑色素瘤的男性患者數目較多 (P=0.042)。大部分葡萄膜黑色素瘤患者進行眼球摘除 (n=12; 92.3%)，而大部分結膜黑色素瘤患者則進行眼眶切除 (n=9; 81.8%)。結膜黑色素瘤的預後遠較葡萄膜黑色素瘤差。葡萄膜黑色素瘤與結膜黑色素瘤的無疾病存活期中位數分別為 5.2年 (範圍, 0.7-20.5) 及2.1年 (範圍, 0.1-24.9)。與葡萄膜黑色素瘤患者相比，結膜黑色素瘤患者與黑色素瘤相關的死亡率顯著較高 (P=0.006)。

**結論：**不論先前的根治性治療如何，香港的結膜黑色素瘤華裔患者的全身轉移及與腫瘤相關的死亡率均高於葡萄膜黑色素瘤。

CM were confirmed by excisional biopsy or analysis of a specimen collected during definitive surgical treatment. Unless refused by the patient, positron emission tomography-computed tomography (PET-CT) scans of UM and CM were performed after 2001 (when such scans became commercially available). Magnetic resonance imaging scans of the brain and orbit, as well as fundus fluorescein angiography and indocyanine green angiography, were conducted to investigate suspected UM. All patients with pathologically confirmed UM or CM underwent definitive surgical treatment. The specific surgical treatment was selected according to melanoma location and size, depth of invasion, systemic metastasis status, and the patient's physical condition.

SPSS software (Windows version 20; IBM Corp, Armonk [NY], US) was utilised for statistical analysis. Differences between patient groups were calculated using the Chi squared and Mann-Whitney *U* tests. *P* values <0.05 were considered statistically significant. Kaplan-Meier survival analysis was performed to estimate disease-free survival and overall survival in patients who had received definitive treatment. Continuous data were reported as mean ± standard deviation.

## Results

In this 25-year retrospective study, there were 13 and

11 patients with pathologically confirmed UM and CM, respectively. Two other patients were excluded: both displayed ocular symptoms (upper eyelid mass and bloody discharge) but were subsequently diagnosed with ocular metastases of primary nasal melanoma. The mean follow-up durations for UM and CM were 67 ± 53.2 and 74 ± 83.3 months, respectively. There were more men among patients with UM than among those with CM (P=0.042). The incidence of pre-existing conjunctival nevus was higher among patients with CM than among those with UM (P=0.049). There were no other significant differences in terms of age at diagnosis, tumour laterality, duration of symptoms, history of ocular nevi, or pathologically determined lesion diameter (Table 1).

Twenty-three of the 24 included patients had visual symptoms on presentation. Among patients with UM, 84.6% (n=11) reported blurring of vision and 7.7% (n=1) presented with photopsia. In one male

patient (7.7%), the tumour was discovered during a routine ophthalmological examination. Patients with CM had more diverse visual symptoms: 63.6% (n=7) exhibited conjunctival pigmentation, 18.2% (n=2) had either an upper or lower eyelid mass, 9.1% (n=1) displayed bloody ocular discharge, and 9.1% (n=1) had experienced bleeding from the mass.

### Tumour staging

Retrospective melanoma staging of UM<sup>9</sup> and CM<sup>10</sup> was conducted in accordance with the AJCC Cancer Staging Manual (8th Edition). Uveal melanoma stages varied from T1a to T4a and from stage I to IIIa. Most UM cases were clinical stage II: 38.5% (n=5), 38.5% (n=5), 7.7% (n=1), and 15.3% (n=2) of patients with UM had clinical stage I, IIA, IIB, and IIIA tumours, respectively. Pathological staging of the tumours revealed that 46.2% (n=6) were spindle cell type, 38.5% (n=5) were epithelioid cell type, and the remaining 15.3% (n=2) were mixed cell type (ie, >10% epithelioid cells and <90% spindle cells). Pathological staging tended to be equivalent to or higher than the initial clinical staging: two patients with pathological stage IIB disease were initially diagnosed with clinical stage I disease, and three patients with pathological stage IIB disease were initially diagnosed with clinical stage IIA disease. For the remaining eight patients, the clinical and pathological stages were identical. Overall, 23.1% (n=3), 15.4% (n=2), 46.2% (n=6), and 15.3% (n=2) of patients with UM had pathological stage I, IIA, IIB and III tumours, respectively.

At diagnosis of CM, the clinical T (cT) stage was cT2 in 72.7% (n=8) of patients and cT3 in 27.3% (n=3) of patients. There were no cT1 or cT4 tumours in our cohort. The pathological T (pT) stage was pT2 in 54.5% (n=6) of patients and pT3 in 45.5% (n=5) of patients. No patients were diagnosed with pT1 or pT4 disease. Unlike the approach or UM, the AJCC staging system for CM does not include guidance regarding overall stage; there is only clinical and pathological staging for the T (tumour) component. One patient had a lower clinical stage (T2b) than pathological stage (T3b); all other patients had identical clinical and pathological stages.

### Disease management

In terms of disease management, biopsies were more frequently performed before definitive treatment in patients with CM than in those with UM (P=0.003). Enucleation was performed in 92.3% (n=12) of patients with UM, whereas orbital exenteration was performed in 81.8% (n=9) of patients with CM. The interventions and treatments performed are shown in Table 2.

After definitive treatment, all patients initially attended weekly follow-up visits; they gradually transitioned to follow-up at 6-month intervals.

TABLE 1. Patient demographics and tumour characteristics\*

	Uveal melanoma (n=13)	Conjunctival melanoma (n=11)	P value
Mean follow-up duration, mo	67 ± 53.2	74 ± 83.3	0.691 <sup>†</sup>
Male sex	9 (69.2%)	3 (27.3%)	0.042 <sup>‡</sup>
Mean age at diagnosis, y	59 ± 15.8 (33-88)	57 ± 13.9 (31-75)	1.000 <sup>†</sup>
Tumour laterality, right eye	7 (53.8%)	6 (54.5%)	1.000 <sup>‡</sup>
History of nevus	1 (7.7%)	3 (27.3%)	0.300 <sup>‡</sup>
No. of Patients with pre-existing conjunctival pigmented lesion	0	3 (27.3%)	0.049 <sup>‡</sup>
Duration of symptoms, mo	7.1 ± 10.9	17.1 ± 19.9	0.400 <sup>†</sup>
Largest diameter of specimen sent, mm	12.4 ± 4.7	10.8 ± 4.0	0.600 <sup>†</sup>

\* Data are shown as No. (%) or mean ± standard deviation (range), unless otherwise specified

<sup>†</sup> Mann-Whitney U test

<sup>‡</sup> Pearson's Chi squared test

TABLE 2. Interventions for uveal and conjunctival melanomas\*

	Uveal melanoma (n=13)	Conjunctival melanoma (n=11)	P value
Biopsy	2 (15.3%)	9 (81.8%)	0.003 <sup>†</sup>
Primary treatment			
Enucleation	12 (92.3%)	-	-
Pars plana vitrectomy and endoresection	1 (7.7%)	-	-
Orbital exenteration	-	9 (81.8%)	-
Wide excisional biopsy with reconstruction	-	2 (18.2%)	-

\* Data are shown as No. (%), unless otherwise specified

<sup>†</sup> Pearson's Chi squared test

Clinical examinations were performed for any surgical complications or disease recurrence. In cases of suspected disease recurrence or metastasis, contrast CT scans of the brain and orbit were performed. No patients with UM or CM had short-term or long-term wound complications. There were no instances of local recurrence during follow-up.

One patient with UM (7.7%) had metastasis to bone, lung, and breast tissue, as determined by high-resolution CT at 105 months of follow-up. The patient died 117 months after initial diagnosis. Two patients (15.3%) died of causes unrelated to melanoma, such as hepatocellular carcinoma or squamous cell carcinoma of the lung.

Patients with CM had worse outcomes than those with had UM, in terms of systemic metastasis ( $P=0.031$ ) and tumour-related mortality rates ( $P=0.006$ ). Overall, 45.5% ( $n=4$ ) of patients with CM developed systemic metastasis during follow-up; the mean time from definitive treatment to systemic metastasis was  $55.8 \pm 66$  months (range, 14-168). Cases were detected when patients were symptomatic and admitted to an acute care hospital for whole-body PET-CT or brain magnetic resonance imaging. Lymph node metastasis in two patients and liver metastasis in one patient were confirmed by fine needle aspiration cytology. Brain metastasis was identified by brain CT in two patients, one of whom had simultaneous bone and lung metastases confirmed by PET-CT. Overall, 18.2% ( $n=2$ ) of patients died of causes unrelated to melanoma. The mean time from definitive treatment to death was  $39 \pm 26$  months (range, 1-64). Patients with CM had shorter median disease-free survival ( $P=0.004$ ) and overall survival ( $P=0.006$ ). Detailed results are presented in Table 3.

At 2 years after definitive treatment, the probabilities of disease-free survival were approximately 0.55 for CM and 1.0 for UM. At 10 years, these probabilities decreased to 0.4 for CM and 0.7 for UM. Overall survival was 100% among patients with UM at 10 years after definitive treatment. In contrast, patients with CM displayed a progressive decrease in overall survival, reaching 35% at 5 years after definitive treatment. Survival curves are depicted in Figures 1 and 2.

## Discussion

To our knowledge, this is the first retrospective study of disease course and outcomes among patients with UM and CM in southern China.

## Demographics

In the present study, the mean ages at diagnosis of UM and CM were 59 and 57 years, respectively. These findings are similar to the ages at diagnosis of UM in Taiwan (55 years)<sup>11</sup> and the US (58 years),<sup>12</sup>

but slightly older than the ages in Singapore (52 years)<sup>13</sup> and South Korea (53 years).<sup>14</sup> The findings are also similar to the ages at diagnosis of CM in the US and mainland China (61 years<sup>15</sup> and 54 years,<sup>16</sup> respectively). It is clear that UM and CM both affect patients in their late 50s to early 60s, regardless of ethnicity.

Uveal melanoma primarily affected men in the present study, consistent with findings in Australian<sup>17</sup> and European<sup>18</sup> Caucasian populations. No previous studies have identified oestrogen receptors in normal uveal tissue or UM tumours,<sup>19</sup> and there is no evidence that oral contraceptives or postmenopausal oestrogens participate in UM aetiology.<sup>20</sup> Because female hormones do not have protective or exacerbating roles in UM, there is speculation that testosterone receptors are present on UM tumours, leading to a higher incidence in men.<sup>21</sup> The present study revealed that CM primarily affected women, but previous studies have not found a relationship between sex and CM incidence.<sup>22,23</sup> In contrast to our results, a study in mainland China showed that CM primarily affected men.<sup>15</sup> Further studies are needed regarding the relationship between sex and CM.

Studies in Caucasian populations have demonstrated that the incidence of UM is much higher than that of CM, with a ratio of approximately 3 to 1.<sup>21,24</sup> In the present study, CM constituted a larger proportion of ocular melanoma cases than previously identified in Caucasian populations, with results similar to epidemiological findings from Korea.<sup>5</sup> Asian populations may have a lower risk of UM, but further research is warranted to confirm this speculation.

## Clinical presentation

Zloto et al<sup>21</sup> described an intriguing phenomenon whereby men were less likely than women to report symptoms of UM. Among our patients with UM, nearly all reported symptoms; one male patient did

TABLE 3. Outcomes of primary uveal and conjunctival melanomas

	Uveal melanoma (n=13)	Conjunctival melanoma (n=11)	P value
Local tumour recurrence	0	0	
Local regional lymph node metastasis	0	2	
Systemic metastasis	1	4	0.031*
Tumour-related mortality	0	5	0.006*
Median disease-free survival, y (range)	5.2 (0.7-20.5)	2.1 (0.1-24.9)	0.004†
Median overall survival, y (range)	5.4 (0.9-20.5)	2.4 (0.2-24.9)	0.006†

\* One-sample *t* test

† Log-rank test

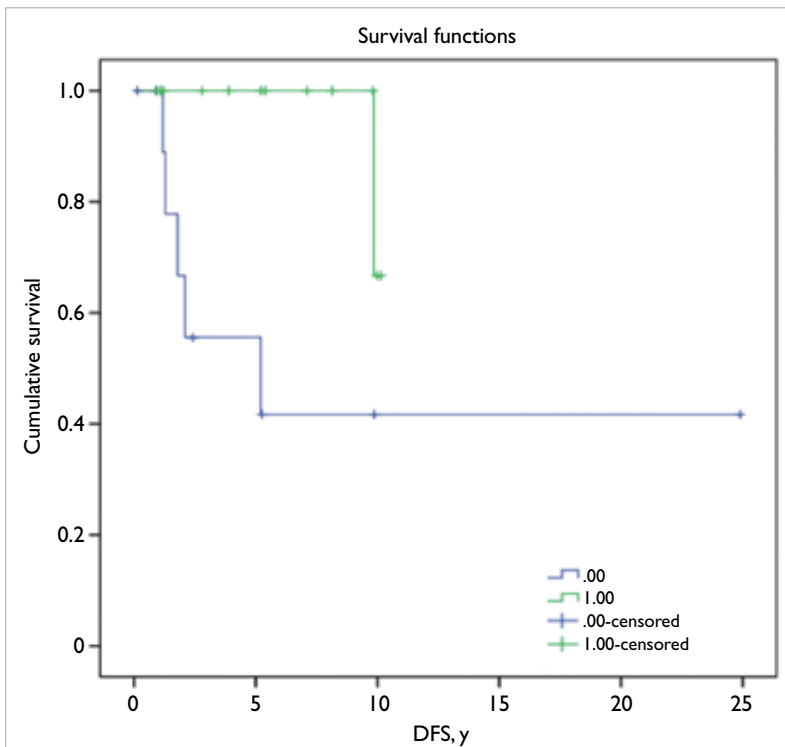


FIG 1. Disease-free survival (DFS) curves for uveal and conjunctival melanomas. Blue line represents conjunctival melanoma and green line represents uveal melanoma; hash marks indicate censoring

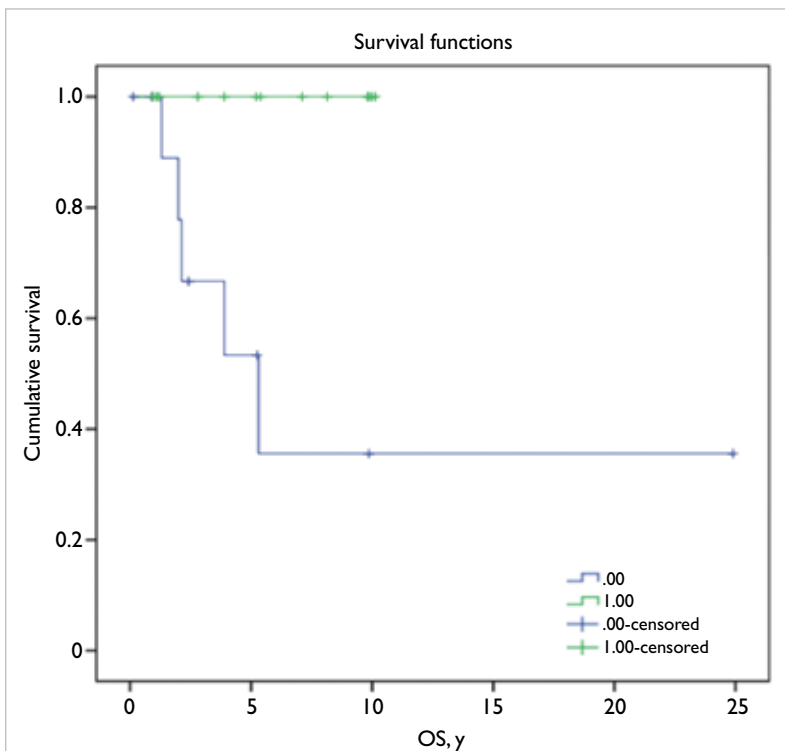


FIG 2. Overall survival (OS) curves for uveal and conjunctival melanomas. Blue line represents conjunctival melanoma and green line represents uveal melanoma; hash marks indicate censoring

not report symptoms and had a tumour identified during a routine examination. Although this finding was not statistically significant, it is consistent with the previous results in a Caucasian population.<sup>2</sup>

In the present study, more patients with CM had pre-existing conjunctival pigmented lesions, compared with those who had UM. Somatic mutations in the *BRAF* gene frequently occur in human melanomas, including CM; such mutations are strongly associated with ultraviolet light exposure.<sup>25</sup> In subtropical regions such as Hong Kong where there is abundant sunlight, analyses of underlying *BRAF* gene mutations could be insightful.

### Tumour staging

Among 10 ophthalmology centres on four continents (North and South America, Europe, and Asia), the proportions of UM stages I, IIA, IIB, and IIIA were 32%, 34%, 22.1%, and 8.8%, respectively<sup>10</sup>; the present study demonstrated a comparatively greater proportion of cases with stage IIB or higher.

Comparative analysis of CM data revealed similar results: patients in the present study had higher clinical stages relative to patients in the US, where three-quarters and more than half of the patients had clinical and pathological stage I disease. This discrepancy could be explained by the rare nature of CM, particularly in Asian populations, leading to lower disease awareness and delayed referral to an ophthalmologist.

### Treatment

Primary enucleation was an effective treatment for patients with UM in the present study; only one patient (7.7%) had systemic metastasis. In that patient, although no systemic metastasis was detected on PET-CT at diagnosis, the maximum standardised uptake value of the UM tumour was particularly high (9.4); UM tumours in other patients had maximum standardised uptake values of 0 to 3.9. Considering the exceptionally high metabolic rate in the UM tumour of the patient with systemic metastasis, microscopic metastasis may have been present before enucleation.

Despite radical treatment with wide excisional biopsy or primary orbital exenteration, systemic metastasis occurred in nearly half of the patients with CM. Regular imaging surveillance by PET-CT may be beneficial for patients with CM after orbital exenteration.

### Prognosis

Among patients with UM, we observed a much lower rate of systemic metastasis than reported in Singapore (7.7% vs 45.5%<sup>26</sup>). This difference could be attributed to the performance of early radical treatment (ie, enucleation) before detection of

systemic metastasis. Notably, the disease-free survival rate was better in our cohort of patients with UM than in another study of Chinese patients with UM (5- and 10-year disease-free survival rates of 80% and 70%, respectively)<sup>27</sup> and better than in a study of Singaporean patients with UM (5-year disease-free survival rate of 56.8%).<sup>13</sup> For comparison, in Caucasian populations, the 5-year and 10-year disease-free survival rates were 81.6%<sup>17</sup> and 50%,<sup>28</sup> respectively.

The rates of systemic metastasis and tumour-related mortality are consistently higher in patients with CM than in those with UM. In the present study, tumour-related mortality at 5 years was similar to the rate in Chinese patients (30.5%)<sup>16</sup> but higher than that among patients in the US (7%).<sup>29</sup> In five large studies (n=734 cases overall) of CM after surgical resection with tumour-free margins, the 5-year overall survival rates ranged from 74% to 86%.<sup>30-34</sup> A recent Singaporean study revealed a slightly lower 5-year overall survival rate (68.8%).<sup>13</sup> In the present study, the 5-year overall survival rate was substantially lower than the rates in other countries. Shields et al<sup>29</sup> reported that a pathologically confirmed positive tumour margin and the absence of limbal involvement were risk factors for CM metastasis. Although all patients with CM in our cohort had pathologically confirmed clear margins, most patients with metastasis (n=6) had palpebral CM (83.3%, n=5) in which the melanoma did not reach the limbus. Thus, tumour location and ethnicity may explain the poor overall survival among patients with CM in the present study.

The higher risk of metastasis and lower rates of 5- and 10-year overall survival in CM, compared with UM, could be attributed to multiple factors. We did not find significant differences between UM and CM in terms of tumour stage or delays in diagnosis/treatment. We suspect that the differences between tumours are related to the nature of the disease, the primary mode of metastasis (UM spreads through the vasculature, whereas CM spreads through the lymphatic system), and genetic alterations (UM is associated with chromosomal abnormalities and CM is associated with mutations in specific genes). In terms of monitoring UM recurrence, the use of single-cell technologies to identify circulating tumour cells has implications for clinical stratification, particularly in cases of UM where specific genetic mutations have been identified.<sup>35</sup> Because circulating tumour cell tests have received US Food and Drug Administration's approval for clinical use in the management of various tumours (eg, metastatic breast and prostate cancers), they may be utilised in future efforts to detect circulating UM tumour cells.

In our centre, sentinel lymph node biopsy (SLNB) is not performed as a component of CM

management. Mor et al<sup>36</sup> recommend SLNB for patients with CM because false-negative findings are rare and 5-year survival can reach 79%. Therefore, early diagnosis of CM, including SLNB in cases with poor prognosticating factors (lack of limbal involvement and positive biopsy margin), and radical neck dissection as appropriate (with support from head and neck surgeons) should be considered before systemic treatment is offered.

### Limitations

This retrospective study included a low number of patients. Additionally, genetic testing was not performed on tissue samples from patients with pathologically confirmed tumours. Chromosomal abnormalities (monosomy 3, gain of chromosome 8q, and monosomy 3 combined with loss of 1p36) have been associated with decreased survival in UM,<sup>37</sup> whereas mutations in the *BRAF*, *RAS*, *ckIT*, and *NF1* genes have been associated with CM<sup>38</sup>; thus, survival could be more closely related to specific genetic features, and it may be inappropriate to consider these tumours as single entities.

### Conclusion

Because UM and CM are rare conditions, they represent challenges for primary physicians (ie, timely referral) and ophthalmologists (ie, appropriate treatment and adequate long-term follow-up). Currently, there is limited information regarding the roles of newer targeted therapies for UM and CM, compared with the application of such therapies to cutaneous melanoma. Among patients with CM, long-term mortality remains high despite definitive radical treatment. This study explored the disease course and outcomes in Hong Kong Chinese patients, then compared the findings with data from patients in other countries. For patients with UM and CM, we recommend long-term follow-up with close monitoring, a detailed medical history, holistic assessment involving cervical and head lymph node palpation, and ophthalmological examination. Collaborations with oncologists to provide regular systemic evaluation during long-term follow-up, with the goal of early detection for distant metastases, are also important. Chest X-ray, brain magnetic resonance imaging, and cytology with SLNB should be performed regularly (annually if possible) to improve survival, particularly in patients with CM.

### Author contributions

Concept or design: HKL Yuen.  
 Acquisition of data: JYY Chan.  
 Analysis or interpretation of data: SC Lam, JYY Chan.  
 Drafting of the manuscript: JYY Chan.  
 Critical revision of the manuscript for important intellectual content: SC Lam, HKL Yuen.

All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

### Conflicts of interest

All authors have disclosed no conflicts of interest.

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### Ethics approval

The study protocol was approved by the Research Ethics Committee (Kowloon Central/Kowloon East) of Hospital Authority, Hong Kong (Ref No.: KC/KE-21-0129/ER-1). Patients were treated in accordance with the tenets of the Declaration of Helsinki, provided written informed consent for all treatments and procedures, and consented to publication of this report.

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## Answers to CME Programme

### *Hong Kong Medical Journal* October 2023 issue

Hong Kong Med J 2023;29:383-95

**I. Twenty-eight-day mortality among patients with severe or critical COVID-19 in Hong Kong during the early stages of the pandemic**

- |   |          |          |          |          |          |
|---|----------|----------|----------|----------|----------|
| A | 1. False | 2. False | 3. False | 4. False | 5. False |
| B | 1. True  | 2. True  | 3. True  | 4. True  | 5. True  |

Hong Kong Med J 2023;29:396-403

**II. Risks and impacts of thromboembolism in patients with pancreatic cancer**

- |   |          |          |          |          |          |
|---|----------|----------|----------|----------|----------|
| A | 1. False | 2. True  | 3. False | 4. False | 5. False |
| B | 1. False | 2. False | 3. True  | 4. False | 5. True  |