Clinical characteristics and prognostic factors of Hurthle cell carcinoma: a population based study

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Abstract

Background: Thyroid Hurthle cell carcinoma (HCC) is a rare disease with high risk of invasion and metastasis and poor prognosis. The clinical characteristics, prognosis and treatment of HCC are still controversial, and clinical data are still limited to some case reports. Therefore, understanding the characteristics and survival factors of HCC is clinically necessary.

Methods: This study collected data from HCC patients diagnosed pathologically from 2004 to 2015, including basic population characteristics, tumor characteristics, and epidemiological and survival data. The data were extracted from the Surveillance, Epidemiology, and End Results (SEER) database to conduct a population cohort study.

Results: A total of 2101 HCC patients with an average age of 55.42 ± 15.27 years were enrolled in this study. Of them, 1740 (82.82%) patients had local disease, 245 (11.66%) had regional disease, and 89 (4.24%) had distant disease. Total thyroidectomy was performed in 1669 (79.44%) patients, partial thyroidectomy was performed in 382 (18.18%) patients, and radioactive iodine (RAI) was used in 1155 (54.97%) patients. The 5-year and 10-year cancer-specific survival rate was 95.4 and 92.6%, respectively. The distant disease group had significantly more male patients, multifocal tumors, and extensive tumors compared to the local disease group. Multivariate survival analysis showed that age (P < 0.05), SEER stage (P < 0.001), and T-stage (P = 0.001) had significant effects on survival. There was no significant difference in survival between total and partial thyroidectomy (P = 0.078), or between RAI and non-RAI (P = 0.733).

Conclusion: Male gender, multifocal tumors, and extended tumors are associated with increased risk of late stage HCC. Age over 45 years, distant SEER stage, and late T-stage are independent risk factors for mortality in HCC.

Keywords: Thyroid Hurthle cell carcinoma, SEER database, Survival factors
Background
Oxyphilic cells, also known as Hurthle cells, are present in some thyroid tumors and nontumor tissues, such as thyroiditis and nodular goiter [1]. Thyroid oxyphilic tumors, also known as Hurthle cell tumors, refer to those thyroid tumors that entirely or predominantly (>75%) consist of oxyphilic thyroid follicular cells [2]. Thyroid oxyphilic tumors have been identified by the World Health Organization as a special type of tumor of the thyroid follicles that are distinguished from thyroid follicular tumors [3]. Thyroid oxyphilic tumors can be benign (Hurthle cell adenoma) or malignant (Hurthle cell carcinoma, HCC). HCC is characterized by capsule invasion and/or vascular invasion. Hurthle cell adenocarcinoma is a rare invasive thyroid malignancy, accounting for 3 to 4% of all thyroid malignancies.

Compared to differentiated thyroid carcinoma, HCC has high risk of lymph node metastasis and distant metastasis and is less sensitive to radioiodine therapy [4, 5]. HCC is a rare disease with unique pathological characteristics and biological behaviors. There is still no consensus on its best surgical treatment method. Our study aimed to find out the characteristics and survival factors of HCC by analyzing patient data from the Surveillance, Epidemiology, and End Results (SEER) database.

Methods
Data collection
All patients diagnosed with oxyphilic adenocarcinoma between 2004 and 2015 according to the International Classification of Disease were identified in the SEER database. Data of patient demographics, surgeries, postoperative treatments, tumor pathology, SEER stage, and disease-specific survival were collected. The SEER stage was used for tumor staging [6].

Statistical analysis
Demographic, tumor features, and treatment methods were summarized with descriptive statistics. Continuous data are presented as means and standard deviations. Categorical data are presented as counts or percentages. Comparisons of the continuous data were made using the one-way ANOVA test followed by the Tukey’s post-hoc test for between three groups or using the independent student t-test for between two groups. Univariate and multivariate Cox proportional hazard models were used to assess the relative impacts of risk factors for HCC. Kaplan-Meier survival curves were constructed for cancer-specific mortality, while the differences between the curves were tested by the log-rank test. All statistical analyses were conducted with SPSS 25.0 (SPSS Inc., Chicago, IL, USA) or GraphPad Prism 7 (GraphPad Software, CA, USA). P < 0.05 was considered statistically significant.

Results
Patient characteristics
A total of 3084 HCC patients were identified in the database, accounting for 2.4% of all differentiated thyroid carcinoma and 6.67% of follicular thyroid carcinoma patients in the same period. Among them, 2101 patients had comprehensive detailed information and were included in the analysis. Patients were divided into three groups according to the SEER stage (local, regional, and distant). The patient characteristics are listed in Table 1.

Comparison of patients with different SEER stages
There was significant difference in age between patients with different SEER stages (P < 0.001; Table 2). The distant group had significantly more patients with male sex (P = 0.001), tumor multifocality (P < 0.001), and tumor extension (P < 0.001) compared to the local group (P < 0.001; Table 2). We also found that the TNM stage was consistent with the SEER stage (Table 2).

Comparison of patients with different surgical procedures
A total of 2051 patients were surgically managed, including 1669 (79.44%) cases of total thyroidectomy and 382 (18.18%) cases of partial thyroidectomy (Table 3). Among the patients undergoing total thyroidectomy, 61.8% were married, versus 54.5% of married patients in the partial thyroidectomy group (P = 0.027). There were significantly more patients with T3, T4, N1, and M1 stages in the total thyroidectomy group than in the partial thyroidectomy group.

Patient survival
The 5-year and 10-year cancer-specific survival (CSS) rates were 95.4 and 92.6%, respectively. Univariate survival analysis showed that age >45 years, late SEER stage, tumor extension, lymph node metastasis, and late TNM stage were associated with poor prognosis (all P < 0.05). Female patients and surgically treated patients had significantly longer survival time (P < 0.001). Multivariate analysis was used to identify the independent prognostic factors. The CSS was 134.36 ± 1.71 months for patients over 45 years of age, and 141.59 ± 1.23 months for patients under 45 years of age, suggesting that age ≥ 45 was an independent prognostic factor (hazard ratio [HR] = 3.595, 95% confidence interval: 1.415–9.131). In addition, regional disease, distant disease, T3 stage, and T4 stage were also independent prognostic factors (HR > 1) (Table 4).

Kaplan-Meier curves were constructed to describe the survival of different groups. Figure 1a shows the CSS of all HCC patients. The 5-year and 10-year
survival rates were 96.53 and 94.77% for female patients, and 92.61 and 86.88% for male patients (Fig. 1b). The 5-year and 10-year survival rates were 98.85 and 98.48% for patients under 45 years of age, and 94.28 and 90.51% for patients over 45 years of age (Fig. 1c). The 5-year and 10-year survival rates were 98.6 and 97.6% for patients with local disease, and 90.8 and 81.7% for patients with regional disease. However, the 5-year and 10-year survival rates were only 46.0 and 26.0% for patients with distant disease (Fig. 1d). The 5-year and 10-year survival rates were 95.6 and 92.7% for patients with negative lymph nodes, which was significantly higher than the 84.9 and 65.3% for those with positive lymph nodes (Fig. 1e). The 10-year survival rates of T1 and T2 stage patients were 97.57 and 98.13%. The 5-year and 10-year survival rates of T3 stage patients was 94.23 and 90.93%, respectively, which were significantly higher than the 5-year and 10-year survival rates of 59.78 and 46.45% for the T4 patients (Fig. 1f). There was no significant difference in 10-year survival rate between patients treated with total thyroidectomy and those treated with partial thyroidectomy (92.6% vs. 95.6%, \( P = 0.078 \)). The 5-year and 10-year survival rates were 61.6 and 46.2% for non-surgically managed patients (Fig. 1g). The 5-year and 10-year survival rates were 96.28 and 93.86% for patients treated with RAI, and 94.18 and 90.78% for patients without RAI (Fig. 1h).

### Table 1 Patient characteristics

| Patient number, n | 2101 |
|-------------------|------|
| **Age, year**     | 55.42 ± 15.27 |
| **Gender, n (%)** |      |
| Male              | 606 (28.84) |
| Female            | 1495 (71.16) |
| **Age, year**     |      |
| < 45              | 508 (24.18) |
| ≥ 45              | 1593 (75.82) |
| **Race, n (%)**   |      |
| White             | 1736 (82.63) |
| Black             | 188 (8.95) |
| American Indian/Alaska Native, Asian/Pacific Islander | 144 (6.85) |
| Unknown           | 33 (1.57) |
| **SEER stage\(^a\), n (%)** |      |
| Local             | 1740 (82.82) |
| Regional          | 245 (11.66) |
| Distant           | 89 (4.24) |
| Unspecified       | 27 (1.28) |
| **Lymph node examination, n (%)** |      |
| Not examined      | 1406 (66.92) |
| Negative          | 574 (27.32) |
| Positive          | 92 (4.38) |
| Unspecified       | 29 (1.38) |
| **Tumor grade, n (%)** |      |
| Well differentiated | 282 (13.42) |
| Moderately differentiated | 80 (3.81) |
| Poorly differentiated | 41 (1.95) |
| Undifferentiated  | 13 (0.62) |
| Unspecified       | 1685 (80.20) |
| **Tumor multifocality\(^b\), n (%)** |      |
| No                | 1657 (78.87) |
| Yes               | 352 (16.75) |
| Unspecified       | 92 (4.38) |
| **Tumor extension, n (%)** |      |
| Intrathyroidal    | 1768 (84.15) |
| Extrathyroidal    | 301 (14.33) |
| Unspecified       | 32 (1.52) |
| **T-stage, n (%)**|      |
| T1                | 486 (23.13) |
| T2                | 707 (33.65) |
| T3                | 708 (33.70) |
| T4                | 98 (4.66) |
| Unspecified       | 102 (4.85) |
| **N-stage, n (%)**|      |
| N0                | 1913 (91.05) |

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\( a\) The local stage includes localized disease only. The regional stage includes regional disease by direct extension only, regional lymph nodes only, and regional disease by both direct extension and lymph node involvement. The distant stage includes disease that involve distant sites and/or lymph nodes.

\( b\) The tumor has multiple centers, and the foci are not contiguous.
Table 2 Patients with different SEER stages

| Characteristics                              | Local disease (n = 1740) | Regional disease (n = 245) | Distant disease (n = 89) | P-value | P²-value | P³-value | P⁴-value |
|----------------------------------------------|--------------------------|---------------------------|-------------------------|---------|---------|---------|---------|
| Age (year)                                   | 54 ± 14.8                | 61 ± 17.1                 | 69 ± 13.5               | < 0.001 | < 0.001 | < 0.001 | < 0.001 |
| Gender, n (%)                                |                          |                           |                         | 0.001   | 0.010   | 0.370   | 0.005   |
| Male                                         | 476 (27.4)               | 87 (35.5)                 | 37 (41.6)               |         |         |         |         |
| Female                                       | 1264 (72.6)              | 158 (64.5)                | 52 (58.4)               |         |         |         |         |
| Race, n (%)                                  |                          |                           |                         | 0.016   | 0.003   | 0.064   | 0.898   |
| White                                        | 1435 (82.5)              | 206 (84.1)                | 72 (82.6)               |         |         |         |         |
| Black                                        | 168 (9.7)                | 9 (3.7)                   | 10 (11.2)               |         |         |         |         |
| American Indian/Alaska Native, Asian/Pacific Islander | 111 (6.4) | 25 (10.2)                | 7 (7.9)                 |         |         |         |         |
| Unknown                                      | 26 (1.5)                 | 5 (2.0)                   | 0                       | < 0.001 | < 0.001 | < 0.001 | < 0.001 |
| Tumor multifocality, n (%)                   |                          |                           |                         | < 0.001 | < 0.001 | < 0.001 | < 0.001 |
| No                                           | 1428 (82.1)              | 173 (70.6)                | 51 (57.3)               |         |         |         |         |
| Yes                                          | 268 (15.4)               | 58 (23.7)                 | 25 (28.1)               |         |         |         |         |
| Unspecified                                  | 44 (2.5)                 | 14 (5.7)                  | 13 (14.6)               |         |         |         |         |
| Tumor extension, n (%)                       |                          |                           |                         | < 0.001 | < 0.001 | 0.023   | < 0.001 |
| Intrathyroidal                                | 1700 (97.7)              | 49 (20.0)                 | 19 (21.3)               |         |         |         |         |
| Extrathyroidal                                | 40 (2.3)                 | 195 (79.6)                | 66 (74.2)               |         |         |         |         |
| Unspecified                                  | 0                        | 1 (0.4)                   | 4 (4.5)                 | < 0.001 | < 0.001 | < 0.001 | < 0.001 |
| T-stage, n (%)                               |                          |                           |                         |         |         |         |         |
| T1                                           | 467 (26.8)               | 16 (6.5)                  | 3 (3.4)                 |         |         |         |         |
| T2                                           | 678 (39.0)               | 21 (8.6)                  | 8 (9.0)                 |         |         |         |         |
| T3                                           | 526 (30.2)               | 164 (66.9)                | 18 (20.2)               |         |         |         |         |
| T4                                           | 1 (0.1)                  | 42 (17.1)                 | 54 (60.7)               | < 0.001 | < 0.001 | < 0.001 | < 0.001 |
| Unspecified                                  | 68 (3.9)                 | 2 (0.8)                   | 6 (6.7)                 | < 0.001 | < 0.001 | 0.023   | < 0.001 |
| N-stage, n (%)                               |                          |                           |                         |         |         |         |         |
| N0                                           | 1703 (97.9)              | 153 (62.4)                | 52 (58.4)               | < 0.001 | < 0.001 | 0.023   | < 0.001 |
| N1                                           | 0                        | 85 (34.7)                 | 28 (31.5)               |         |         |         |         |
| Unspecified                                  | 37 (2.1)                 | 7 (2.9)                   | 9 (10.1)                | < 0.001 | 0.167   | < 0.001 | < 0.001 |
| M-stage, n (%)                               |                          |                           |                         |         |         |         |         |
| M0                                           | 1718 (98.7)              | 240 (98.0)                | 30 (33.7)               | < 0.001 | 0.167   | < 0.001 | < 0.001 |
| M1                                           | 0                        | 0                        | 59 (66.3)               |         |         |         |         |
| Unspecified                                  | 22 (1.3)                 | 5 (2.0)                   | 0                       |         |         |         |         |

SEER: Surveillance, Epidemiology, and End Results. P¹, local stage vs. regional stage; P², regional stage vs. distant stage; P³, local stage vs. distant stage

Discussion
Our study analyzed the basic characteristics, treatment methods, and survival of patients with HCC. From 2000 to 2015, 86 patients with thyroid Hurthle cell tumors were treated at the Peking Union Medical College Hospital, of which only 5 patients were diagnosed with thyroid HCC. Most literatures on HCC are case reports rather than clinical studies with large samples. Moreover, diagnosis of HCC relies on postoperative pathology. HCC is also characterized by multifocality with high risk of lymph node metastases and distant metastases [7]. Approximately 10–20% of patients have metastases when diagnosed with HCC. Up to 37% of extrathyroidal extension HCC metastasizes to the cervical lymph nodes [8]. There is still no consensus on the optimal treatment method for HCC, and the postoperative effect of radioactive iodine treatment is unclear.

The SEER database has been utilized to find the differences between HCC and other thyroid cancers [9–11]. Compared to other differentiated thyroid cancers, HCC is more aggressive with higher risk of distant metastasis and poor prognosis. For the first time, our study used the data of 2101 patients in the SEER database from 2004 to 2015 to describe the clinical characteristics of HCC patients and identify the prognostic factors of CSS.
HCC is more common in women with a male to female ratio of approximately 1:2 to 1:4 [1], which is similar to our result of the ratio of male to female of 1:2.47. The first symptoms of HCC patients may include thyroid nodules or cervical lymphadenectomy. The SEER staging plays an important role in the treatment and

| Characteristics                        | Total thyroidectomy (n = 1669) | Partial thyroidectomy (n = 382) | P-value |
|----------------------------------------|-------------------------------|--------------------------------|---------|
| Age                                    | 55 ± 15.0                     | 55 ± 16.5                       | 0.136   |
| Gender, (%)                            |                               |                                | 0.556   |
| Male                                   | 484 (29.0)                    | 105 (27.5)                      |         |
| Female                                 | 1185 (71.0)                   | 277 (72.5)                      |         |
| Race, n (%)                            |                               |                                | 0.667   |
| White                                  | 1387 (83.1)                   | 309 (80.9)                      |         |
| Black                                  | 148 (8.9)                     | 36 (9.4)                        |         |
| American Indian/Alaska Native, Asian/Pacific Islander | 113 (6.8) | 30 (7.9) |         |
| Unknown                                | 21 (1.3)                      | 7 (1.8)                         |         |
| SEER stage, n (%)                      |                               |                                | 0.023   |
| Local                                  | 1388 (83.2)                   | 340 (89.0)                      |         |
| Regional                               | 208 (12.5)                    | 35 (9.2)                        |         |
| Distant                                | 68 (4.1)                      | 6 (1.6)                         |         |
| Unspecified                            | 5 (0.3)                       | 1 (0.3)                         |         |
| Tumor multifocality, n (%)             |                               |                                | 0.072   |
| No                                     | 1324 (79.3)                   | 317 (83.0)                      |         |
| Yes                                    | 295 (17.7)                    | 50 (13.1)                       |         |
| Unspecified                            | 50 (3.0)                      | 15 (3.9)                        |         |
| Tumor extension, n (%)                 |                               |                                | 0.394   |
| Intrathyroidal                         | 1420 (85.1)                   | 335 (87.7)                      |         |
| Extrathyroidal                         | 241 (14.4)                    | 46 (12.0)                       |         |
| Unspecified                            | 8 (0.5)                       | 1 (0.3)                         |         |
| T-stage, n (%)                         |                               |                                | 0.022   |
| T1                                     | 391 (23.4)                    | 93 (24.3)                       |         |
| T2                                     | 566 (33.9)                    | 137 (35.9)                      |         |
| T3                                     | 577 (34.6)                    | 122 (31.9)                      |         |
| T4                                     | 80 (4.8)                      | 8 (2.1)                         |         |
| Unspecified                            | 55 (3.3)                      | 22 (5.8)                        |         |
| N-stage, n (%)                         |                               |                                | < 0.001 |
| N0                                     | 1535 (92.0)                   | 361 (94.5)                      |         |
| N1                                     | 99 (5.9)                      | 6 (1.6)                         |         |
| Unspecified                            | 35 (2.1)                      | 15 (3.9)                        |         |
| M-stage, n (%)                         |                               |                                | 0.005   |
| M0                                     | 1605 (96.2)                   | 368 (96.3)                      |         |
| M1                                     | 44 (2.6)                      | 3 (0.8)                         |         |
| Unspecified                            | 20 (1.2)                      | 11 (2.9)                        |         |
| Radiotherapy, n (%)                    |                               |                                | < 0.001 |
| No                                     | 557 (33.4)                    | 262 (68.6)                      |         |
| Radioactive iodine                     | 1033 (61.9)                   | 111 (29.1)                      |         |
| Unspecified                            | 79 (4.7)                      | 9 (2.4)                         |         |

SEER: Surveillance Epidemiology and End Results
| Features                  | Univariate      | Multivariate    | P-value | Univariate      | Multivariate    | P-value |
|---------------------------|-----------------|-----------------|---------|-----------------|-----------------|---------|
|                           | HR (95% CI)     | P-value         | HR (95% CI) | P-value         | HR (95% CI)     | P-value |
| Gender                    |                 |                 |          |                 |                 |         |
| Male                      | 1               | 1               |          | 1               | 1               |         |
| Female                    | 0.415 (0.278–0.619) | < 0.001         | 0.614 (0.409–0.924) | 0.019 |
| Age (year)                |                 |                 |          |                 |                 |         |
| < 45                      | 1               | 1               |          | 1               | 1               |         |
| ≥ 45                      | 6.354 (2.582–15.635) | < 0.001         | 4.204 (1.695–10.432) | 0.002 |
| Race                      |                 |                 |          |                 |                 |         |
| White                     | 1               | –               |          | –               | –               |         |
| Black                     | 0.960 (0.465–1.984) | 0.913          | –       | –               | –               |         |
| Other                     | 0.646 (0.237–1.761) | 0.393          | –       | –               | –               |         |
| SEER stage                |                 |                 |          |                 |                 |         |
| Local                     | 1               | 1               |          | 1               | 1               |         |
| Regional                  | 8.454 (4.823–14.817) | < 0.001         | 8.015 (4.555–14.101) | < 0.001 |
| Distant                   | 61.625 (3.772–31.568) | < 0.001        | 46.219 (27.108–78.804) | < 0.001 |
| Tumor multifocality       |                 |                 |          |                 |                 |         |
| No                        | 1               | –               |          | –               | –               |         |
| Yes                       | 1.334 (0.808–2.202) | 0.260          | –       | –               | –               |         |
| Tumor extension           |                 |                 |          |                 |                 |         |
| Intrathyroidal            | 1               | –               |          | –               | –               |         |
| Extrathyroidal            | 12.342 (8.062–18.892) | < 0.001        | –       | –               | –               |         |
| Lymph node examination    |                 |                 |          |                 |                 |         |
| Not examined              | 1               | –               |          | –               | –               |         |
| Negative                  | 1.060 (0.646–1.741) | 0.817          | –       | –               | –               |         |
| Positive                  | 6.029 (3.494–10.403) | < 0.001        | –       | –               | –               |         |
| T-stage                   |                 |                 |          |                 |                 |         |
| T1                        | 1               | –               |          | –               | –               |         |
| T2                        | 0.701 (0.226–2.173) | 0.538          | –       | –               | –               |         |
| T3                        | 4.866 (2.060–11.496) | < 0.001        | –       | –               | –               |         |
| T4                        | 42.305 (7.874–100.132) | < 0.001        | –       | –               | –               |         |
| N-stage                   |                 |                 |          |                 |                 |         |
| N0                        | 1               | –               |          | –               | –               |         |
| N1                        | 8.863 (5.561–14.124) | < 0.001        | –       | –               | –               |         |
| M-stage                   |                 |                 |          |                 |                 |         |
| M0                        | 1               | –               |          | –               | –               |         |
| M1                        | 32.934 (21.214–51.129) | < 0.001        | –       | –               | –               |         |
| Surgery                   |                 |                 |          |                 |                 |         |
| No                        | 1               | 1               |          | 1               | 1               |         |
| Total thyroidectomy       | 0.085 (0.044–0.166) | < 0.001        | 0.335 (0.152–0.741) | 0.007 |
| Partial thyroidectomy     | 0.046 (0.019–0.114) | < 0.001        | 0.266 (0.096–0.742) | 0.011 |
| Radiotherapy              |                 |                 |          |                 |                 |         |
| No                        | 1               | –               |          | –               | –               |         |
| Yes                       | 0.606 (0.405–0.905) | 0.014          | –       | –               | –               |         |

CI confidence interval, SEER Surveillance Epidemiology and End Results
Fig. 1 Survival analysis. (a) Cancer-specific survival of the patients. (b) Cancer-specific survival of patients under and over 45 years of age ($P = 0.007$). (c) Cancer-specific survival of patients with different SEER stages ($P < 0.001$). (d) Cancer-specific survival of patients with different lymph node status ($P < 0.001$). (e) Cancer-specific survival of patients with different T stages ($P < 0.001$). (F) Cancer-specific survival of surgically and non-surgically managed patients ($P < 0.001$).
prognosis of HCC. Therefore, our study also analyzed the relationship between the HCC clinical characteristics and SEER staging. The SEER staging integrates clinical and pathological data to provide accurate evaluation of the degree of disease. Our study found that older age, male sex, multifocal tumors, and extensive tumors were risk factors of late SEER stages. These results suggest that HCC has similar characteristics with other differentiated thyroid carcinomas.

Surgery is still the most effective treatment for HCC [10, 12]. Our study found no significant difference in CSS between patients treated with total thyroidectomy and those treated with partial thyroidectomy. This result suggests that the cancer-specific prognosis of HCC is not greatly affected by surgical methods. We speculate that partial thyroidectomy is sufficient for single, small tumors without extrathyroidal invasion. Compared with total thyroidectomy, partial thyroidectomy has fewer complications and less intraoperative injury, but has comparable survival time.

Radioactive iodine (RAI) is widely used for the treatment of differentiated thyroid cancer, especially papilla thyroid carcinoma. However, HCC is insensitive to RAI due to the low iodine uptake rate. Despite this, RAI is used in some patients after total thyroidectomy [13]. The multivariate Cox analysis found that RAI treatment did not significantly improve the prognosis of HCC. However, the univariate Cox analysis showed that HCC patients can benefit from RAI treatment, which is consistent with previous findings [12].

HCC is associated with a higher metastasis rate and a lower survival rate compared to other differentiated thyroid cancers [14]. HCC with distant metastases has a 5-year mortality rate of up to 80% [15]. Age, tumor size, and sex are prognostic factors of HCC, and tumor extension and recurrence often indicate poor prognosis and increased mortality [16]. The reported 5-year and 10-year survival rates for nonmetastatic HCC are 85.1 and 71.1%, respectively [17]. In our study, the 5-year and 10-year CSS rate for HCC were 95.4 and 92.6%, respectively. The higher survival rates in our study may be explained by the advancement in diagnosis and treatment of HCC in the last decade.

Our study has limitations. First, a small portion of the included patients had no data of race or tumor characteristics. For example, 80.2% of the patients had unclear tumor grades, and 2–5% had unclear TNM stages. Therefore, the SEER stage was adopted to describe the disease progression rather than the TNM stage. Second, the tumor grade data was excluded from the analysis due to incomplete information. Third, the SEER database has no detailed information on tumor multifocality, tumor extension, and completion thyroidectomy.

Conclusions
The SEER stage is an independent prognostic factor for HCC, and distant disease is associated with significantly poor prognosis. Age over 45 years, distant SEER stage, and late T-stage are independent risk factors for mortality in HCC. There was no significant difference in survival between patients treated with partial thyroidectomy and those treated with total thyroidectomy. RAI treatment may possibly improve patient survival after thyroidectomy.

Abbreviations
HCC: Hurthle cell carcinoma; SEER: Surveillance, Epidemiology, and End Results

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Ethics approval and consent to participate
The study protocol was approved by the Ethics Committee of Peking Union Medical College Hospital. Informed consent to participate was waived by the Ethics Committee because no patients were enrolled in this study.

Consent for publication
Informed consent for publication was waived because all data analyzed in this paper are anonymous. Availability of data and material: The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests
The authors declare that they have no competing interests.

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References
1. Johnson TL, et al. Hurthle cell thyroid tumors. An immunohistochemical study. Cancer. 1987;59(1):107–12.
2. Hanief MR, Igali L, Grana D. Hurthle cell carcinoma: diagnostic and therapeutic implications. World J Surg Oncol. 2004;2:27.
3. Sheffield, E.A., Armed forces institute of pathology, atlas of tumor pathology: 3rd Series. Tumors of the thyroid gland. J. Rosai, M. L. Carcangiu and R. A. Delailllis. Armed Forces Institute of Pathology, Washington, DC, 1992. No. of pages: 343. Price: $58. ISBN: 1 881041 03 4. The Journal of Pathology, 1993 171(3): p. 247–248.
4. Guerrero MA, et al. Age and tumor size predicts lymph node involvement in Hurthle cell carcinoma. J. Cancer. 2010;1:23–6.
5. Bishop JA, et al. Histological patterns of locoregional recurrence in Hurthle cell carcinoma of the thyroid gland. Thyroid. 2012;22(7):690-4.
6. Jr, Y.J., et al., SEER Summary Staging Manual –2000: Codes and Coding Instructions, National Cancer Institute, NIH Pub. No. 01–4969, Bethesda, MD, 2001., 2001.
7. Ghosein RA, et al. Prognostic factors of recurrence in encapsulated Hurthle cell carcinoma of the thyroid gland: a clinicopathologic study of 50 cases. Cancer. 2006;106(8):1669–76.
8. Stojadinovic A, et al. Hurthle cell carcinoma: a critical histopathologic appraisal. J Clin Oncol. 2001;19(10):2616–25.
9. Nagar S, et al. Hurthle cell carcinoma: an update on survival over the last 35 years. Surgery. 2013;154(6):1263–71 discussion 1271.
10. Kuo EJ, Roman SA, Sosa JA. Patients with follicular and Hurthle cell microcarcinomas have compromised survival: a population level study of 22,738 patients. Surgery. 2013;154(6):1246–53 discussion 1253-4.
11. Goffredo P, Roman SA, Sosa JA. Hurthle cell carcinoma: a population-level analysis of 3311 patients. Cancer. 2013;119(3):504–11.
12. McHenry CR, Sandoval BA. Management of follicular and Hurthle cell neoplasms of the thyroid gland. Surg Oncol Clin N Am. 1998;7(4):893–910.
13. Besic N, et al. The role of radioactive iodine in the treatment of Hurthle cell carcinoma of the thyroid. Thyroid. 2003;13(6):577–84.
14. Carcangiu ML, et al. Follicular Hurthle cell tumors of the thyroid gland. Cancer. 1991;68(9):1944–53.
15. Kushchayeva Y, et al. Prognostic indications for Hurthle cell cancer. World J Surg. 2004;28(12):1266–70.
16. Lopez-Penabad L, et al. Prognostic factors in patients with Hurthle cell neoplasms of the thyroid. Cancer. 2003;97(5):1186–94.
17. Bhattacharyya N. Survival and prognosis in Hurthle cell carcinoma of the thyroid gland. Arch Otolaryngol Head Neck Surg. 2003;129(2):207–10.

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