



Incidence of patients with bone metastases at diagnosis of solid tumors in adults: a large population-based study

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Background: Bones are one of the most common metastatic sites for solid malignancies. Bone metastases can significantly increase mortality and decrease the quality of life of cancer patients. In the United States, around 350,000 people die each year from bone metastases. This study aimed to analyze and update the incidence and prognosis of bone metastases with solid tumors at the time of cancer diagnosis and its incidence rate for each solid cancer.

Methods: We used the Surveillance, Epidemiology, and End Results (SEER) database to find patients diagnosed with solid cancers originating from outside the bones and joints between 2010 and 2016. Data were stratified by age, sex, and race. Patients with a tumor *in situ* or with an unknown bone metastases stage were excluded. We then selected most of the sites where cancer often occurred, leaving 2,207,796 patients for the final incidence analysis. For the survival analysis, patients were excluded if they were diagnosed at their autopsy or on their death certificate, or had unknown follow-ups. The incidence of bone metastases and overall survival was compared between patients with different primary tumor sites.

Results: We identified 2,470,634 patients, including 426,594 patients with metastatic disease and 113,317 patients with bone metastases, for incidence analysis. The incidence of bone metastases among the metastatic subset was 88.74% in prostate cancer, 53.71% in breast cancer, and 38.65% in renal cancer. In descending order of incidence, there were patients with other cancers in the genitourinary system (except for renal, bladder, prostate, and testicular cancer) (37.91%), adenocarcinoma of the lung (ADC) (36.86%), other gynecologic cancers (36.02%), small-cell lung cancer (SCLC) (34.56%), non-small cell lung cancer not otherwise specified and others [NSCLC (NOS/others)] (33.55%), and bladder (31.08%) cancers. The rate of bone metastases is 23.19% in SCLC, 22.50% in NSCLC (NOS/others), 20.28% in ADC, 8.44% in squamous cell carcinoma of the lung (SCC), and 4.11% in bronchioloalveolar carcinoma [NSCLC (BAC)]. As for the digestive system, the overall bone metastases rate was 7.99% in the esophagus, 4.47% in the

gastric cancer, 4.42% in the hepatobiliary cancer, 3.80% in the pancreas, 3.26% in other digestive organs, 1.24% in the colorectum, and 1.00% in the anus. Overall, the incidence rate of bone metastases among the entire cohort in breast and prostate cancer was 3.73% and 5.69%, respectively.

Conclusions: The results of this study provide population-based estimates for the incidence rates of patients with bone metastases at initial diagnosis of their solid tumor. The findings can help clinicians to early detect bone metastases by bone screening to anticipate the occurrence of symptoms and favorably improve the prognosis.

Keywords: Bone metastases; Surveillance, Epidemiology, and End Results (SEER); incidence; prognosis

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Introduction

Bones are one of the most common sites of metastases for many types of solid cancers (1-4). Bone metastases have an increased risk of serious skeletal-related events (SREs), such as pathological fractures, pain, hypercalcemia, and spinal cord compressions, which can seriously impair patients' quality of life (5-9). Bone metastases also lead to a significant increase in mortality and morbidity (10-12).

In the United States, around 350,000 people die each year from bone metastasis (13). Several patients with bone metastasis and SREs are affected by breast or prostate cancer, while lower rates are observed in patients with lung, kidney, thyroid, or other cancers (4,14). The incidence rate of bone metastases in the United States is still unknown, and estimates have varied from 21,000–400,000 per annum. Though bone metastases can impact the mortality and quality of life of patients with cancer, more extensive population-based studies researching the incidence and prognosis of patients with bone metastases are lacking. Previous studies have shown that the prevalence of bone metastases is more than 70% in patients with metastatic breast and prostate cancer, and approximately 30% in metastatic renal cell carcinoma (1,12,15-18). However, there are no studies which provide information on the incidence of bone metastasis in other common cancers or systemic malignancies. Also, earlier studies cannot reflect the recent incidence and survival trends of patients with bone metastases (19).

Our study was conducted to estimate the incidence and prognosis of patients with bone metastases using the Surveillance, Epidemiology, and End Results (SEER) database that includes information on cancer incidence, treatment, and survival for approximately 30% of the

American population (20). Specifically, we estimated the incidence proportion of patients' bone metastases among solid tumors, considering tumor histology at the time of initial diagnosis.

Methods

Data source and cohort population

For our study, the SEER database was used. Inclusion criteria were adult patients (age ≥ 18 years) with a diagnosis of an invasive solid tumor originating outside of the bone and joints between January 1, 2010, and December 31, 2016. Patients were excluded if information relating to the presence or absence of bone metastases was unavailable. Other exclusion criteria were patients with diagnosis of carcinoma *in situ* and patients with a diagnosis of a rare tumor such as thymus cancer, heart cancer, mediastinum cancer, pleura cancer, spleen cancer, reticuloendothelial cancer, skin cancer, connective and soft tissue cancer, adrenal gland cancer, parathyroid gland cancer, other endocrine gland cancer, mesothelioma, Kaposi sarcoma, and lymphoma. For the survival analysis, patients were excluded if they were diagnosed at the time of the autopsy or at the issuing of the death certificate, or if they had unknown survival time or survival status.

Statistical analysis

Total numbers and incidence proportions of patients who were diagnosed with bone metastases were computed and then stratified by cancer type. The patients with lung cancer were classified by tumor histology using the International Classification of Disease for Oncology,

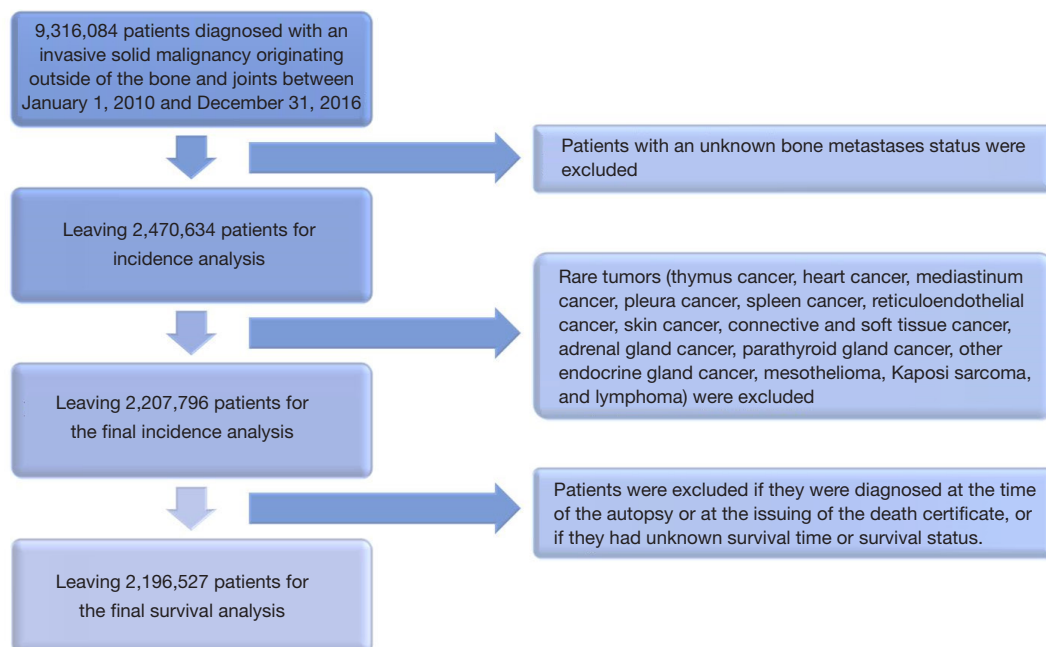


Figure 1 Selection of study patients.

3rd Edition (ICD-O-3). Metastatic stage was conducted following the 7th edition of the American Joint Committee on Cancer staging manual, and then we defined patients with metastatic cancer as a subset with metastatic disease. We defined patients with bone metastases as a subset with bone metastases. The incidence proportion was defined as the number of patients diagnosed with bone metastases and a specific primary cancer divided by the total number of individuals diagnosed with that primary cancer; we also defined a second incidence proportion in which the denominator was restricted to patients with metastatic disease. The metastatic status of the brain, lung, and liver was also available, and we used it to characterize the extent of systemic disease, and subsequently calculated the incidence and median survival of patients with bone metastases classified by the extent of systemic disease. For survival estimates, we used the Kaplan-Meier method, taking into account a P value ≤ 0.05 as significant. The statistical analysis was generated and visualized with SPSS software (version 18; IBM Corp., USA).

Results

First, we identified 9,316,084 patients aged ≥ 18 years who were diagnosed with an invasive solid malignancy originating outside of the bone and joints between January

1, 2010 and December 31, 2016. The SEER database includes information on cancer incidence, treatment, and survival for approximately 30% of the American population. Patients were excluded in the cohort if the carcinoma was in situ. Patients with an unknown bone metastases stage were excluded, leaving 2,470,634 patients for analysis. We then selected most of the sites where cancer often occurred, leaving 2,207,796 patients for the final incidence analysis (Figure 1).

Between 2010–2016, a total of 2,207,796 patients had a diagnosis of cancer from common solid organs, and 426,594 patients had metastatic disease. We found 113,317 patients with bone metastases, which accounted for 5.13% of all patients, and 26.56% of those patients had metastatic disease.

Next, we found that the rate of bone metastases varied widely by primary cancer type (Table 1; Figure 2). As shown in Table 1, the bone metastasis rate is the highest in lung cancer. More specifically, the rate of bone metastases is 23.19% for small-cell lung cancer (SCLC), 22.50% in non-small cell lung cancer not otherwise specified and others [NSCLC (NOS/others)], 20.28% for adenocarcinoma of the lung (ADC), 8.44% in squamous cell carcinoma of the lung (SCC), and 4.11% in bronchioloalveolar carcinoma [NSCLC (BAC)]. In analyzing the gastrointestinal tumors, the rate of bone metastases is 7.99% in the esophagus,

Table 1 Incidence proportion and median survival of patients with identified bone metastases at diagnosis by primary cancer site

| Site | Sub-site | Number of patients with cancer (any stage) | Number of patients with metastatic disease | Number of patients with bone metastases at diagnosis | Incidence proportion of bone metastases among entire cohort (%) | Incidence proportion of bone metastases among subset with metastatic disease (%) | Incidence proportion of bone metastases among subset with metastatic disease (%) | Median survival in months (interquartile range) among patients with bone metastases (months) |
|----------------------------|----------------------------|--|--|--|---|--|--|--|
| Head and neck ¹ | Head and neck ¹ | 77,610 | 11,267 | 1,114 | 1.44 | 9.89 | 9.89 | 8 [3–18] |
| Thyroid | Thyroid | 88,356 | 3,347 | 679 | 0.77 | 20.29 | 20.29 | 23 [4–82] |
| Breast | Breast | 436,347 | 30,285 | 16,266 | 3.73 | 53.71 | 53.71 | 27 [8–57] |
| Respiratory system | SCLC | 39,765 | 26,686 | 9,223 | 23.19 | 34.56 | 34.56 | 5 [1–10] |
| | SCC | 93,240 | 33,839 | 7,867 | 8.44 | 23.25 | 23.25 | 3 [1–7] |
| | ADC | 147,194 | 80,981 | 29,846 | 20.28 | 36.86 | 36.86 | 5 [1–13] |
| | NSCLC (BAC) | 4,475 | 1,024 | 184 | 4.11 | 17.97 | 17.97 | 7 [3–20] |
| | NSCLC (NOS/ others) | 20,622 | 13,224 | 4,434 | 21.50 | 33.53 | 33.53 | 3 [1–8] |
| Digestive system | Esophagus | 25,955 | 10,005 | 2,075 | 7.99 | 20.74 | 20.74 | 11 [4–36] |
| | Gastric | 43,570 | 15,525 | 1,947 | 4.47 | 12.54 | 12.54 | 3 [1–8] |
| | Hepatobiliary | 72,015 | 16,454 | 3,186 | 4.42 | 19.36 | 19.36 | 3 [1–7] |
| | Pancreatic | 74,660 | 39,535 | 2,835 | 3.80 | 7.17 | 7.17 | 2 [1–6] |
| | Colorectal | 249,273 | 52,311 | 3,085 | 1.24 | 5.90 | 5.90 | 5 [1–15] |
| | Anal | 12,150 | 1,584 | 121 | 1.00 | 7.64 | 7.64 | 3 [NR–7] |
| | Other digestive organs | 23,514 | 8,229 | 767 | 3.26 | 9.32 | 9.32 | 3 [1–8] |
| Genitourinary | Renal | 101,121 | 14,498 | 5,630 | 16.08 | 38.65 | 38.65 | 6 [2–17] |
| | Bladder | 124,279 | 5,921 | 1,840 | 1.48 | 31.08 | 31.08 | 4 [1–10] |
| | Prostate | 346,844 | 22,257 | 19,750 | 5.69 | 88.74 | 88.74 | 25 [11–55] |
| | Testicular | 16,661 | 1,993 | 143 | 0.86 | 7.18 | 7.18 | NR [7–NR] |
| | Other GU | 8,467 | 757 | 287 | 3.39 | 37.91 | 37.91 | 4 [1–9] |

Table 1 (continued)

Table 1 (continued)

| Site | Sub-site | Number of patients with cancer (any stage) | Number of patients with metastatic disease | Number of patients with bone metastases at diagnosis | Incidence proportion of bone metastases among entire cohort (%) | Incidence proportion of bone metastases among subset with metastatic disease (%) | Median survival in months (interquartile range) among patients with bone metastases (months) |
|--------------------------------|--------------------------------|--|--|--|---|--|--|
| Gynecologic | Ovarian | 37,468 | 23,890 | 422 | 1.13 | 1.77 | 5 [1–17] |
| | Endometrial | 93,149 | 8,304 | 847 | 0.91 | 10.20 | 6 [2–15] |
| | Cervical | 22,774 | 3,585 | 558 | 2.45 | 15.56 | 6 [2–15] |
| Brain and other nervous system | Other gynecologic | 15,160 | 497 | 179 | 1.18 | 36.02 | 6 [2–16] |
| | Brain and other nervous system | 33,127 | 596 | 59 | 0.18 | 9.90 | 15 [3–NR] |

¹, lip, tongue, gum, floor of mouth, & other mouth, salivary gland, oropharynx, nasopharynx, hypopharynx, pharynx, nasal cavity (including nasal cartilage), accessory sinuses, middle & inner ear, larynx, trachea, orbit & lacrimal gland, retina, eyeball, eye, NOS. GI, gastrointestinal; GU, genitourinary; GYN, gynecologic; SCLC, small-cell lung cancer; NSCLC (NOS/others), non-small cell lung cancer not otherwise specified or non-small cell lung cancer other lung cancer; ADC, adenocarcinoma of the lung; SCC, squamous cell carcinoma of the lung; NSCLC (BAC), bronchioloalveolar carcinoma; NR, not reached.

4.47% in the gastric system, 4.42% in the hepatobiliary system, 3.80% in the pancreas, 3.26% in other digestive organs, 1.24% in colorectum, and 1.00% in the anus. Among patients with renal cancer, prostate and breast cancer, 16.08%, 5.69%, and 3.73% of patients were respectively found to have bone metastases.

Moreover, *Table 1* and *Figure 3* show the incidence proportion of patients with bone metastases among the metastatic subset (patients with stage IV disease at diagnosis). The incidence of bone metastases among the metastatic subset is 88.74% in prostate cancer, 53.71% in breast cancer, and 38.65% in renal cancer. In descending order, patients with other cancers of the genitourinary system (except renal, bladder, prostate, testicular) (37.91%), ADC (36.86%), other gynecologic cancers (except ovarian, endometrial, and endometrial cancer) (36.02%), SCLC (34.56%), NSCLC (NOS/others) (33.55%), and bladder cancer (31.08%), showed an incidence proportion of bone metastases of >30%.

Table 1 and *Figure 4* show the median survival time of patients with bone metastases in different systemic malignancies. The median survival time among patients with breast cancer and bone metastases, prostate cancer, and bone metastases and thyroid cancer, and bone metastases are 27, 25, and 23 months, respectively. The survival time of the 3 cancers mentioned above is higher than the others. The median survival time of other tumors with bone metastases is less than 10 months. In general, survival is worse in patients with digestive system cancer and bone metastases compared with other types of primary cancer. The median survival time in patients with hepatobiliary, gastric, and anal tumors is 3 months. Among patients with pancreatic tumor and bone metastases, the median survival time is 2 months.

Incidence proportion and median survival time of patients with bone metastases, as organized based on the presence or absence of brain, liver, and lung metastases, are shown in *Table 2*. In summary, the incidence of bone metastasis was higher, and survival time was shorter among patients with more extensive metastases at diagnosis. The incidence of bone-only metastasis was 13.98% in NSCLC (NOS/others), 12.64% in SCLC, and 11.81% in ADC. In descending order, patients with bladder cancer (5.14%), SCC (4.90%), esophageal cancer (4.52%), gastric cancer (2.86%), hepatobiliary cancer (2.74%), renal cancer (2.65%), breast cancer (2.22%), and NSCLC (BAC) (2.02%) showed an incidence proportion of bone metastases of >2%. The median survival time among patients with bone-only

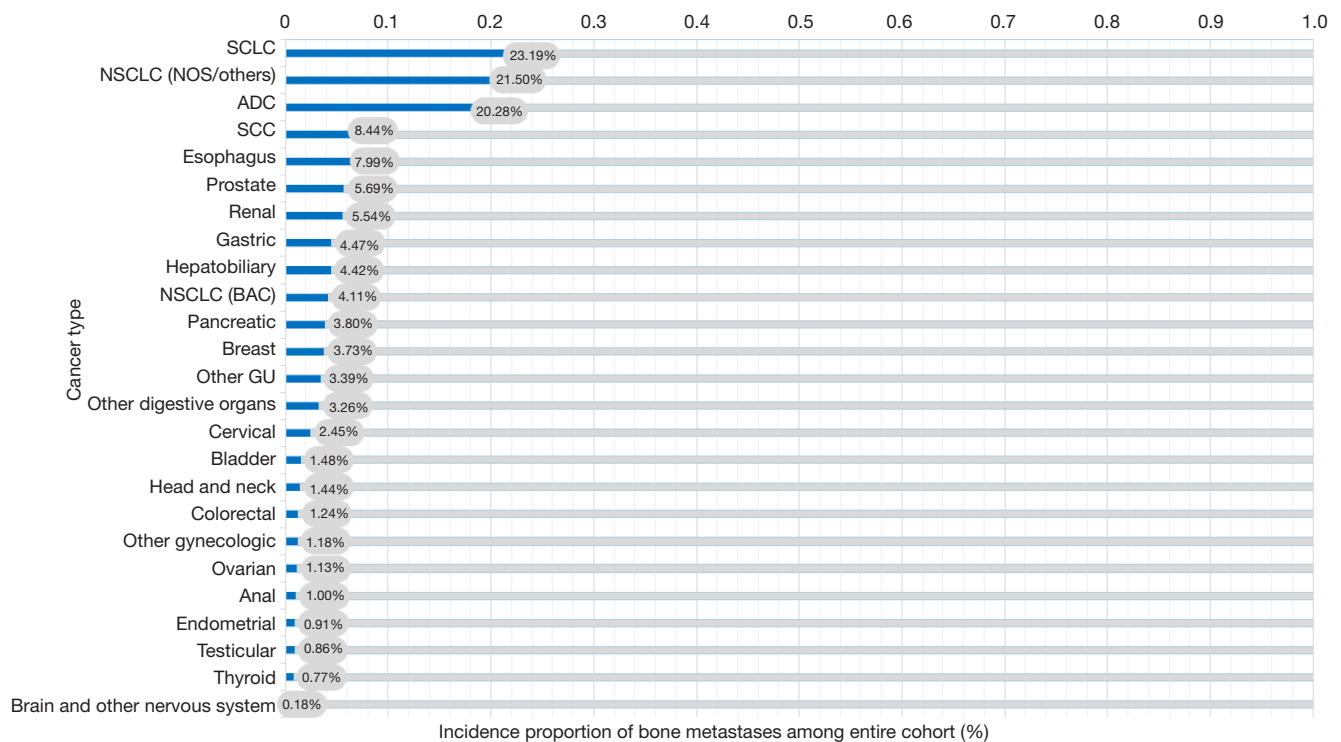


Figure 2 Incidence proportion of patients diagnosed with bone metastases within the entire cohort. SCLC, small-cell lung cancer; NSCLC, non-small cell lung cancer; BAC, bronchioloalveolar carcinoma; NOS, not otherwise specified; ADC, adenocarcinoma of the lung; SCC, squamous cell carcinoma of the lung; GI, gastrointestinal; GU, genitourinary; GYN, gynecologic.

metastases in thyroid cancer, breast cancer, prostate cancer, and anal cancer was 60, 35, 27, and 20 months, respectively.

For patients with head and neck cancer, the incidence of comorbidity with liver metastases and bone metastasis was 42.47%. Among patients with was cancer, the incidence of comorbidity with liver metastasis and bone metastasis is higher in NSCLC (BAC) (54.17%), ADC (53.73%), and NSCLC (NOS/others) (44.10%) than in SCC (39.59%) and SCLC (37.15%). Furthermore, we found that the incidence of comorbidity of brain metastases and bone metastasis was higher than other sites among patients with digestive system cancer and gynecologic cancer.

Table S1 shows the incidence proportions of patients diagnosed with bone metastases, classified according to primary cancer, age, race, and gender. Median survival estimates, and those of age, race, gender, and cancer type, are displayed in Table S2.

Discussion

In our study, we showed the number and incidence

proportion of patients with bone metastases and the prognosis of identified bone metastases among patients with cancer of the digestive system with the lowest median survival time. To our knowledge, this is the first epidemiologic study of bone metastases using the entire SEER database. Roodman *et al.* pointed out that the exact prevalence of bone metastasis remains unknown, and patients with bone metastases are usually incurable (21). Therefore, it is probable that our study may have widespread applications and could be useful in the formation of screening paradigms for bone metastases, clinical treatment and trial design, and counseling of different subsets of patients with cancer.

Incidence of bone metastasis

In 1997, Coleman *et al.* reported that the incidence of bone metastasis was 30–40% for patients with lung cancer, which is higher than our results (22). In 2013, Sathiakumar *et al.* reported that the incidence of bone metastasis among lung cancer patients was 19.8%, based on data from 1999 to

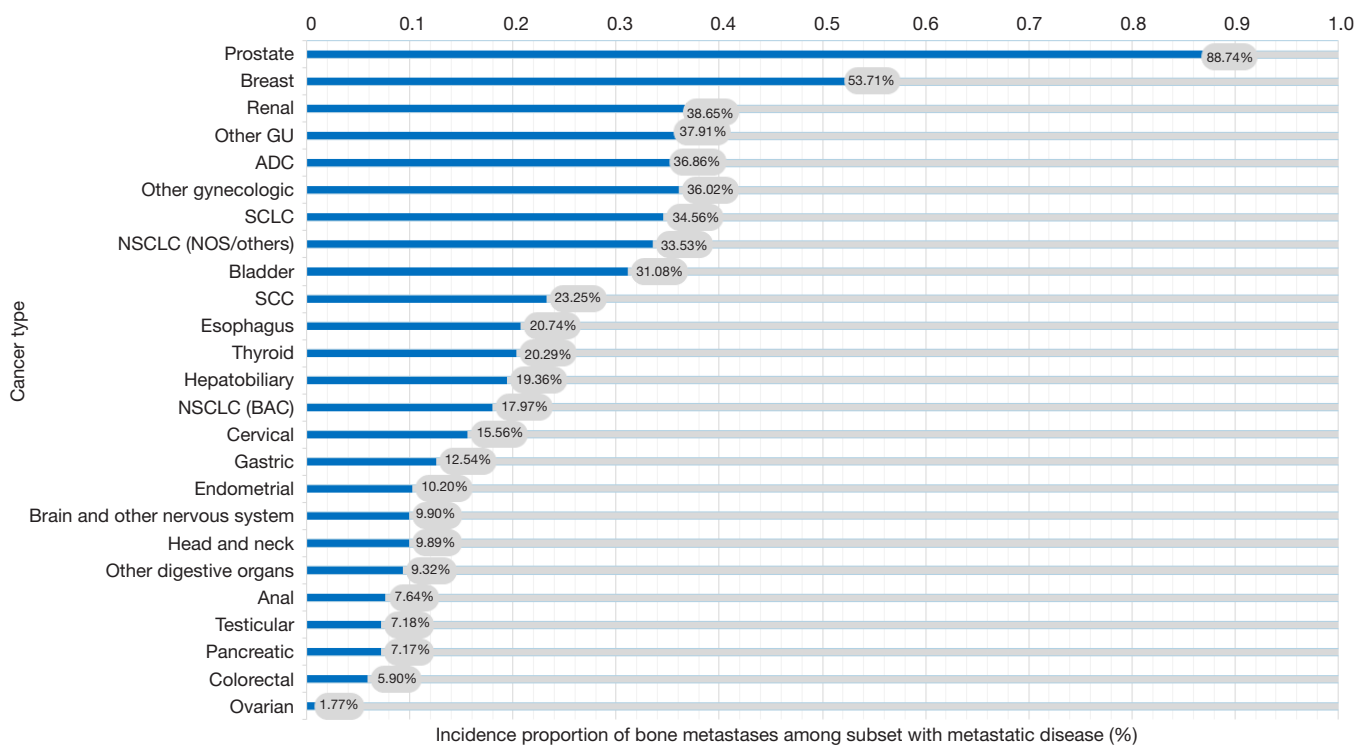


Figure 3 Incidence proportion of patients diagnosed with bone metastases within subset with metastatic disease. SCLC, small-cell lung cancer; NSCLC, non-small cell lung cancer; BAC, bronchioloalveolar carcinoma; NOS, not otherwise specified; ADC, adenocarcinoma of the lung; SCC, squamous cell carcinoma of the lung; GI, gastrointestinal; GU, genitourinary; GYN, gynecologic.

2006 (23). Al Husaini *et al.* pointed out that the incidence of skeletal metastasis in advanced-stage lung cancer was 30–40% (24).

In our study, we found that the incidence of bone metastases was 16.89% in patients with newly diagnosed lung cancer and 33.10% in patients with metastatic lung cancer. A comparison of our findings with those of other studies confirms that the rate of bone metastasis among lung cancer is gradually decreasing, which has contributed to the popularization of screening and the development of effective treatment strategies. Additionally, we found the incidence of bone metastases among patients with SCLC to be higher than that of patients with non-small cell lung cancer (NSCLC). Yerushalmi *et al.* found that the incidence of bone metastases among patients with breast cancer had decreased steadily over 3 time periods (25) (1989–1991: 7.5%, 1992–1997: 5.3%, 1998–2001: 3.5%). Jensen *et al.* noted that the incidence rate of bone metastases among patients with breast cancer was 3.6% in a population of 35,912 patients (19). In this study, the incidence was slightly lower than that reported by earlier studies. Pietropaoli *et al.*

indicated that only approximately 1% of patients with stage IV carcinoma of the head and neck had concomitant bone metastases (26), which is similar to our results.

Previous studies have reported that the incidence rate of bone metastases in patients with hepatocellular carcinoma ranges from 3% to 20% (27,28). These findings are consistent with our results. However, the studies just mentioned above only discussed the incidence rate of bone metastases in single cancers. There is no study which systematically analyzes the incidence of bone metastases in different cancer types. Our study shows that lung cancer is most likely to present with bone metastasis, which may support recent screening guidelines. Previous studies have shown that the incidence rate of bone metastases in metastatic prostate cancer is over 80%, while bone metastases occur in 65–80% of patients with metastatic breast cancer (29–34). Our study also indicates that the incidence proportion of bone metastases is high in patients with breast or prostate cancer. Previous studies have shown that bone metastases occur in approximately 30% of patients with invasive bladder cancer and renal cancer

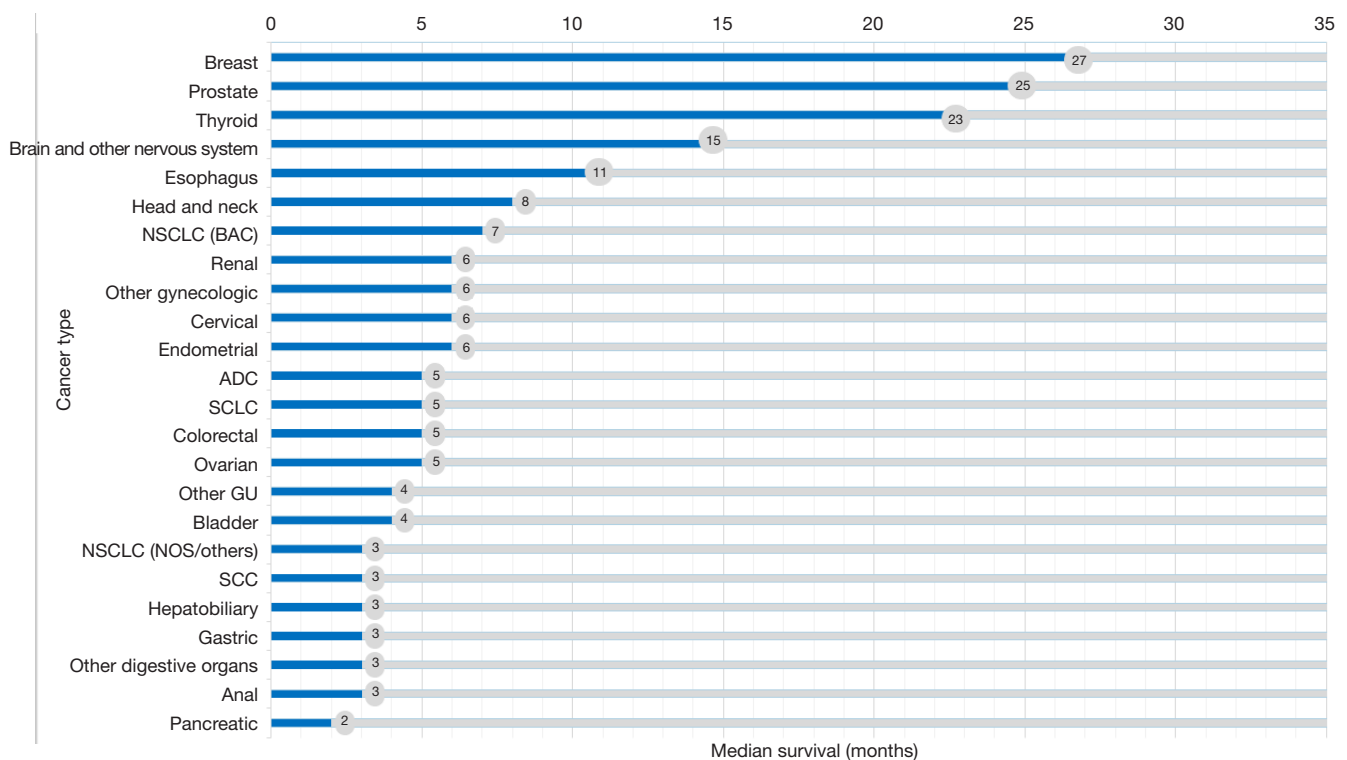


Figure 4 Median survival of patients with identified bone metastases. SCLC, small-cell lung cancer; NSCLC, non-small cell lung cancer; BAC, bronchioloalveolar carcinoma; NOS, not otherwise specified; ADC, adenocarcinoma of the lung; SCC, squamous cell carcinoma of the lung; GI, gastrointestinal; GU, genitourinary; GYN, gynecologic.

(35–38). In our study, the incidence rate of bone metastases was 16.08% and 1.48% in renal cancer and bladder cancer, respectively. Furthermore, bone metastases accounted for 38.65% and 31.08% of metastatic renal and bladder cancers, respectively. Though the rate of bone metastases is not high in bladder cancer, bone cancer accounts for a relatively large portion of the metastatic sites among patients with metastatic bladder cancer. Therefore, we must pay attention to the screening of bone metastases in this setting.

Survival

Our results show that cancer presented at diagnosis with bone metastases with the longest median survival time is breast cancer (27 months), followed by prostate cancer (25 months), and thyroid cancer (23 months). Previous studies had shown that the median survival time is 30 and 28 months among breast cancer patients with bone metastases and prostate cancer patients with bone metastases (39,40). These results are similar to ours. Bhatia reported that the prognosis of hepatocellular carcinoma with bone

metastasis is extremely poor, with a median survival of only 1–2 months (41). We also found that the median survival time is the shortest in cancers of the digestive system. Silvestris *et al.* indicated that the median survival was 6 months in gastric cancer patients after bone metastasis diagnosis (42). Our results showed the median survival is 3 months among gastric cancer patients with bone metastases, which was a little shorter than the earlier study.

Clinical implications

Bone metastases are associated with an increased risk of mortality for patients with cancer and may lead to a poor quality of life (17,43,44). The early detection of bone metastases may minimize morbidity and mortality and lead to a better quality of life (45–47), while also being a fundamental step in anticancer treatment (48–50). The National Comprehensive Cancer Network (NCCN) clinical practice guidelines in oncology also recommended routine screening bone metastases in patients with SCLC, prostatic cancer, and high-metastasis-risk renal cancer (51–54). Our results support

Table 2 Incidence proportion and median survival of patients with bone metastases by extent of systemic disease

| Site | Sub-site | Type of systemic metastasis | Number of patients | Number of patients with bone metastases | Proportion with bone metastases (%) | Median survival in months (interquartile range) |
|----------------------------|----------------------------|-----------------------------|--------------------|---|-------------------------------------|---|
| Head and neck ¹ | Head and neck ¹ | Lung | 1,284 | 217 | 16.90 | 6 [3–13] |
| | | Liver | 372 | 158 | 42.47 | 8 [3–18] |
| | | Brain | 77 | 21 | 27.27 | 5 [1–18] |
| | | 2 of 3 | 273 | 122 | 44.69 | 4 [2–12] |
| | | All 3 | 18 | 12 | 66.67 | 5 [1–13] |
| | | None | 75,371 | 532 | 0.71 | 10 [4–23] |
| Thyroid | Thyroid | Lung | 1,076 | 224 | 20.82 | 11 [2–49] |
| | | Liver | 95 | 31 | 32.63 | 4 [1–13] |
| | | Brain | 48 | 17 | 35.42 | 5 [2–NR] |
| | | 2 of 3 | 142 | 63 | 44.37 | 5 [2–12] |
| | | All 3 | 8 | 5 | 62.50 | 2 [1–6] |
| | | None | 86,987 | 339 | 0.39 | 60 [12–NR] |
| Breast | Breast | Lung | 4,926 | 2,414 | 49.01 | 24 [7–50] |
| | | Liver | 3,690 | 2,042 | 55.34 | 18 [4–42] |
| | | Brain | 752 | 418 | 55.59 | 15 [4–34] |
| | | 2 of 3 | 2,504 | 1,692 | 67.57 | 11 [2–30] |
| | | All 3 | 349 | 280 | 80.23 | 4 [1–17] |
| | | None | 424,126 | 9,415 | 2.22 | 35 [14–69] |
| Respiratory system | SCLC | Lung | 2,279 | 523 | 22.95 | 6 [1–11] |
| | | Liver | 7,849 | 2,916 | 37.15 | 5 [1–9] |
| | | Brain | 3,489 | 580 | 16.62 | 5 [2–10] |
| | | 2 of 3 | 3,930 | 1,710 | 43.51 | 4 [1–8] |
| | | All 3 | 517 | 299 | 57.83 | 3 [1–7] |
| | | None | 20,444 | 2,584 | 12.64 | 7 [2–12] |
| | SCC | Lung | 6,065 | 1,051 | 17.33 | 3 [1–7] |
| | | Liver | 2,445 | 968 | 39.59 | 3 [1–6] |
| | | Brain | 2,354 | 490 | 20.82 | 3 [1–6] |
| | | 2 of 3 | 1,904 | 832 | 43.70 | 2 [1–5] |
| | | All 3 | 284 | 160 | 56.34 | 2 [1–4] |
| | | None | 79,077 | 3,877 | 4.90 | 4 [1–9] |

Table 2 (continued)

Table 2 (continued)

| Site | Sub-site | Type of systemic metastasis | Number of patients | Number of patients with bone metastases | Proportion with bone metastases (%) | Median survival in months (interquartile range) | |
|--------|------------------------|-----------------------------|--------------------|---|-------------------------------------|---|-----------|
| | ADC | Lung | 14,485 | 4,233 | 29.22 | 5 [2–14] | |
| | | Liver | 5,265 | 2,829 | 53.73 | 3 [1–9] | |
| | | Brain | 11,839 | 3,357 | 28.36 | 5 [2–14] | |
| | | 2 of 3 | 8,273 | 4,402 | 53.21 | 3 [1–10] | |
| | | All 3 | 1,353 | 990 | 73.17 | 3 [1–9] | |
| | | None | 102,527 | 12,106 | 11.81 | 6 [2–15] | |
| | NSCLC (BAC) | Lung | 352 | 38 | 10.80 | 11 [4–15] | |
| | | Liver | 24 | 13 | 54.17 | 2 [1–10] | |
| | | Brain | 53 | 15 | 28.30 | 10 [3–19] | |
| | | 2 of 3 | 55 | 27 | 49.09 | 7 [3–21] | |
| | | All 3 | 3 | 1 | 33.33 | 6 [NA] | |
| | | None | 3,953 | 80 | 2.02 | 11 [3–23] | |
| | NSCLC (NOS/ others) | Lung | 1,881 | 538 | 28.60 | 3 [1–8] | |
| | | Liver | 1,093 | 482 | 44.10 | 2 [1–7] | |
| | | Brain | 2,124 | 485 | 22.83 | 3 [1–8] | |
| | | 2 of 3 | 1,358 | 604 | 44.48 | 2 [1–5] | |
| | | All 3 | 223 | 129 | 57.85 | 2 [1–4] | |
| | | None | 13,306 | 1,860 | 13.98 | 4 [1–9] | |
| | Digestive system | Esophagus | Lung | 1,242 | 239 | 19.24 | 10 [4–42] |
| | | | Liver | 2,722 | 505 | 18.55 | 10 [3–30] |
| | | | Brain | 228 | 58 | 25.44 | 9 [4–30] |
| | | | 2 of 3 | 1,206 | 310 | 25.70 | 11 [4–43] |
| | | | All 3 | 87 | 38 | 43.68 | 14 [7–NR] |
| | | | None | 20,470 | 925 | 4.52 | 13 [4–36] |
| | | Gastric | Lung | 979 | 191 | 19.51 | 4 [1–7] |
| | | | Liver | 5,342 | 406 | 7.60 | 3 [1–9] |
| | | | Brain | 137 | 34 | 24.82 | 3 [1–4] |
| 2 of 3 | | | 1,186 | 267 | 22.51 | 2 [NR–8] | |
| All 3 | | | 52 | 22 | 42.31 | 3 [1–4] | |
| None | | | 35,874 | 1,027 | 2.86 | 4 [1–9] | |

Table 2 (continued)

Table 2 (continued)

| Site | Sub-site | Type of systemic metastasis | Number of patients | Number of patients with bone metastases | Proportion with bone metastases (%) | Median survival in months (interquartile range) |
|--------|------------------------|-----------------------------|--------------------|---|-------------------------------------|---|
| | Hepatobiliary | Lung | 3,238 | 472 | 14.58 | 2 [0–6] |
| | | Liver | 4,598 | 399 | 8.68 | 3 [1–9] |
| | | Brain | 125 | 45 | 36.00 | 4 [1–10] |
| | | 2 of 3 | 1,314 | 298 | 22.68 | 2 [1–5] |
| | | All 3 | 36 | 17 | 47.22 | 2 [0–7] |
| | | None | 61,751 | 1,692 | 2.74 | 3 [1–8] |
| | Pancreatic | Lung | 2,846 | 304 | 10.68 | 6 [2–19] |
| | | Liver | 23,754 | 1,140 | 4.80 | 5 [1–14] |
| | | Brain | 71 | 16 | 22.54 | 2 [1–7] |
| | | 2 of 3 | 5,011 | 762 | 15.21 | 1 [0–4] |
| | | All 3 | 92 | 40 | 43.48 | 2 [0–3] |
| | | None | 42,886 | 573 | 1.34 | 3 [1–9] |
| | Colorectal | Lung | 3,425 | 261 | 7.62 | 6 [2–18] |
| | | Liver | 26,849 | 1,102 | 4.10 | 5 [1–14] |
| | | Brain | 190 | 18 | 9.47 | 2 [1–7] |
| | | 2 of 3 | 8,472 | 983 | 11.60 | 5 [1–14] |
| | | All 3 | 205 | 68 | 33.17 | 2 [1–10] |
| | | None | 210,132 | 653 | 0.31 | 6 [2–18] |
| | Anal | Lung | 129 | 11 | 8.53 | 6 [5–8] |
| | | Liver | 317 | 26 | 8.20 | 9 [4–27] |
| | | Brain | 9 | 1 | 11.11 | NA |
| | | 2 of 3 | 116 | 15 | 12.93 | 4 [1–9] |
| | | All 3 | 3 | 0 | 0.00 | NA |
| | | None | 11,576 | 68 | 0.59 | 20 [6–36] |
| | Other digestive organs | Lung | 748 | 122 | 16.31 | 2 [1–7] |
| | | Liver | 3,714 | 255 | 6.87 | 3 [1–11] |
| | | Brain | 66 | 15 | 22.73 | 2 [1–6] |
| 2 of 3 | | 728 | 179 | 24.59 | 2 [0–5] | |
| All 3 | | 36 | 16 | 44.44 | 1 [0–2] | |
| None | | 18,222 | 269 | 1.48 | 3 [1–11] | |

Table 2 (continued)

Table 2 (continued)

| Site | Sub-site | Type of systemic metastasis | Number of patients | Number of patients with bone metastases | Proportion with bone metastases (%) | Median survival in months (interquartile range) |
|---------------|------------|-----------------------------|--------------------|---|-------------------------------------|---|
| Genitourinary | Renal | Lung | 5,624 | 1,605 | 28.54 | 6 [2–15] |
| | | Liver | 1,237 | 372 | 30.07 | 3 [1–9] |
| | | Brain | 449 | 137 | 30.51 | 5 [2–15] |
| | | 2 of 3 | 2,360 | 949 | 40.21 | 3 [1–8] |
| | | All 3 | 219 | 118 | 53.88 | 3 [1–7] |
| | | None | 91,232 | 2,422 | 2.65 | 10 [3–30] |
| | Bladder | Lung | 1,437 | 1,131 | 78.71 | 4 [1–10] |
| | | Liver | 660 | 485 | 73.48 | 2 [1–6] |
| | | Brain | 184 | 154 | 83.70 | 2 [1–11] |
| | | 2 of 3 | 359 | 286 | 79.67 | 2 [1–5] |
| | | All 3 | 24 | 19 | 79.17 | 1 [0–2] |
| | | None | 344,200 | 17,675 | 5.14 | 5 [2–12] |
| | Prostate | Lung | 1,133 | 191 | 16.86 | 20 [8–47] |
| | | Liver | 497 | 148 | 29.78 | 10 [4–22] |
| | | Brain | 724 | 68 | 9.39 | 10 [3–24] |
| | | 2 of 3 | 1,185 | 345 | 29.11 | 9 [3–24] |
| | | All 3 | 347 | 164 | 47.26 | 14 [4–NR] |
| | | None | 277,125 | 296 | 0.11 | 27 [11–57] |
| | Testicular | Lung | 883 | 44 | 4.98 | NR [8–NR] |
| | | Liver | 87 | 12 | 13.79 | 9 [7–19] |
| | | Brain | 14 | 1 | 7.14 | NA |
| | | 2 of 3 | 261 | 30 | 11.49 | 13 [4–NR] |
| | | All 3 | 56 | 8 | 14.29 | 8 [0–NR] |
| | | None | 15,360 | 48 | 0.31 | NR [8–NR] |
| | Other GU | Lung | 217 | 48 | 22.12 | 5 [2–12] |
| | | Liver | 155 | 50 | 32.26 | 2 [0–6] |
| | | Brain | 14 | 5 | 35.71 | 4 [1–7] |
| | | 2 of 3 | 110 | 44 | 40.00 | 1 [0–6] |
| | | All 3 | 4 | 0 | 0.00 | NA |
| | | None | 7,967 | 140 | 1.76 | 7 [2–11] |

Table 2 (continued)

Table 2 (continued)

| Site | Sub-site | Type of systemic metastasis | Number of patients | Number of patients with bone metastases | Proportion with bone metastases (%) | Median survival in months (interquartile range) |
|--------------------------------|--------------------------------|-----------------------------|--------------------|---|-------------------------------------|---|
| Gynecologic | Ovarian | Lung | 1,515 | 60 | 3.96 | 4 [1–19] |
| | | Liver | 1,928 | 72 | 3.73 | 2 [0–11] |
| | | Brain | 56 | 10 | 17.86 | NR [NR–10] |
| | | 2 of 3 | 650 | 88 | 13.54 | 4 [1–9] |
| | | All 3 | 17 | 8 | 47.06 | 2 [NR–6] |
| | | None | 33,302 | 184 | 0.55 | 7 [1–34] |
| | Endometrial | Lung | 1,898 | 225 | 11.85 | 7 [2–18] |
| | | Liver | 638 | 66 | 10.34 | 6 [2–15] |
| | | Brain | 87 | 15 | 17.24 | 2 [2–6] |
| | | 2 of 3 | 593 | 156 | 26.31 | 3 [1–9] |
| | | All 3 | 36 | 18 | 50.00 | 3 [1–10] |
| | | None | 89,897 | 337 | 0.37 | 8 [2–19] |
| | Cervical | Lung | 702 | 116 | 16.52 | 6 [3–13] |
| | | Liver | 250 | 63 | 25.20 | 6 [2–11] |
| | | Brain | 35 | 15 | 42.86 | 3 [1–6] |
| | | 2 of 3 | 259 | 103 | 39.77 | 4 [1–9] |
| | | All 3 | 8 | 5 | 62.50 | 3 [1–10] |
| | | None | 21,514 | 256 | 1.19 | 10 [4–20] |
| | Other gynecologic | Lung | 457 | 47 | 10.28 | 4 [1–10] |
| | | Liver | 187 | 17 | 9.09 | 6 [3–14] |
| | | Brain | 9 | 1 | 11.11 | 2 [2–2] |
| | | 2 of 3 | 137 | 17 | 12.41 | 2 [0–5] |
| | | All 3 | 13 | 3 | 23.08 | 1 [NR] |
| | | None | 14,357 | 94 | 0.65 | 8 [3–22] |
| Brain and other nervous system | Brain and other nervous system | Lung | 32 | 4 | 12.50 | 19 [3–NR] |
| | | Liver | 14 | 4 | 28.57 | 1 [NR–8] |
| | | Brain | 200 | 4 | 2.00 | 3 [NR] |
| | | 2 of 3 | 9 | 2 | 22.22 | 4 [NR–8] |
| | | All 3 | NA | NA | NA | NA |
| | | None | 32,872 | 45 | 0.14 | 16 [2–NR] |

¹, lip, tongue, gum, floor of mouth, & other mouth, salivary gland, oropharynx, nasopharynx, hypopharynx, pharynx, nasal cavity (including nasal cartilage), accessory, sinuses, middle & inner ear, larynx, trachea, orbit & lacrimal gland, retina, eyeball, eye, NOS. GI, gastrointestinal; GU, genitourinary; GYN, gynecologic; SCLC, small-cell lung; NSCLC (NOS/others), non-small cell lung cancer not otherwise specified or non-small cell lung cancer other lung cancer; ADC, adenocarcinoma of the lung; SCC, squamous cell carcinoma of the lung; NSCLC (BAC), bronchioloalveolar carcinoma; NR, not reached; NA, not applicable.

the current guidelines as these cancers are all at high risk of the development of bone metastases, although the routine use of bone screening is not recommended in NSCLC. Our data showed that the incidence of bone metastases at diagnosis in NSLCLC is relatively high. Therefore, in patients with a diagnosis of stage IV NSCLC, special focus should be dedicated to the screening of the bones.

Furthermore, screening of bone metastases is not routinely performed for patients with esophagus cancer (55). However, our data revealed a 7.99% and 20.74% incidence proportion of bone metastases in patients with esophagus cancer and metastatic esophagus cancer, respectively. Therefore, routine screening of bone metastases is necessary for patients with these cancers.

As screening was not routinely performed in these patients, bone metastases are always discovered only as a result of SREs, which may be a more advanced disease that shortens survival (56) and often requires surgical intervention or a more complex treatment plan. However, surgery for pathological fracture and loss of motor function and mobility might also increase mortality (5). Our data show a relatively high rate of bone metastasis in these populations—one which may be underestimated. Therefore, our findings may support the need to routinely screen for bone metastases at diagnosis for these patients.

As for patients with head and neck cancers, the incidence of comorbidity for liver metastasis and bone metastases is high. Patients with breast and bladder cancer have a high incidence of comorbidity with bone metastasis and brain, liver, or lung metastasis. Therefore, a diagnosis of bone metastases may be a strong signal that other sites of metastases may exist in patients. For lung cancer, we should pay attention to the comorbidity of bone metastases and liver metastases, while for digestive system cancer and gynecologic cancer, we may be more concerned about the comorbidity of bone metastases and brain metastases.

Previous studies have shown that patients with bone-only metastases have a better prognosis (57-59). For instance, previous investigators pointed out that the median survival time of patients with breast cancer and bone-only metastasis was about 20–50 months, which is much longer than multiple sites metastasis (60-63). This result is consistent with our findings. The incidence of bone-only metastasis is high in NSCLC (NOS/others), SCLC, ADC, bladder cancer, and esophageal cancer. So, for patients with these cancers, we must find a specific metastasis status. Because the treatment of bone-only metastasis is different from other sites or multiple sites metastasis (60), identifying bone-

only metastasis may help clarify the clinical course, improve the prognosis for patients with bone-only metastasis, and estimate median survival time more accurately (64,65).

Our data also have value for the design of clinical trials. The data in our study may help investigators quantify the specific number of patients needed to be excluded from the trial enrollment, with bone metastasis as an exclusion criterion. Moreover, for studies or trials which are related to bone metastases, our study can provide generalizable estimates of incidence and prognosis for use in calculations and some trial design.

Limitations

The present study has some potential limitations. Firstly, we only identified bone metastases at initial cancer diagnosis, and, because SEER cannot provide information relating to disease recurrence, we could not screen patients with bone metastases after initial diagnosis. Secondly, we do not have information relating to the number size and exact location of the bone metastases. Thirdly, screening was not conducted across all malignancies, and therefore some data of metastases might have been missed. Finally, treatment information for the metastatic sites was not provided, so we could not study the treatment received by each patient.

Although this study has several limitations, it provides new information regarding the epidemiology of bone metastasis. Incidence of bone metastasis and the specific proportion of patients with bone metastases among different cancer types could help in the development of the formation of screening paradigms for bone metastases, clinical treatment and trial design, and counseling of different subsets of patients with cancer.

Conclusions

The results of this study provide population-based estimates of the incidence of bone metastasis and the specific incidence proportion of patients with bone metastasis diagnosis of solid tumors. We have shown that prostate cancer and breast cancer are most likely to occur with bone metastases. Additionally, the rate of bone metastasis was more than 20% in patients with lung, renal, bladder, thyroid, and esophageal cancers. We also found that the median survival time was more than 20 months in bone metastatic breast cancer, prostate cancer, and thyroid cancer. Conversely, the median survival time was the shortest in gastrointestinal, lung, and gynecologic cancer

with bone metastases. These data may help clinicians in their justification of using of bone screening, which may also have an important role in clinical trial design and better prognosis. The findings can support the decision of screening of the bone and extracranial metastases for patients with high-risk primary malignancy.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <http://dx.doi.org/10.21037/atm.2020.03.55>). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Table S1 Incidence proportion of patients with identified bone metastases at diagnosis by primary cancer site as stratified by age, race, and gender

| Site | Sub-site | Age | | | | Race | | | | Gender | | | | | | | | | |
|--------------------------|-----------------------------------|-----------------------|---|---------------|---|--|-------------------------------|---|-------------------------------|---|--|--------|--|-------------------------|------------------------------|--|---|-------|-------|
| | | Age category in years | Number of patients with bone metastases | Entire cohort | Incidence proportion of bone metastases among entire cohort (%) | Incidence proportion of bone metastases among subset with metastatic disease (%) | Race | Number of patients with bone metastases | Entire cohort | Incidence proportion of bone metastases among entire cohort (%) | Incidence proportion of bone metastases among subset with metastatic disease (%) | Gender | Number of patients with brain metastases (total number of patients in subcategory) | Number of entire cohort | Number of metastatic disease | Incidence proportion of brain metastases among entire cohort | Incidence proportion of brain metastases among subset with metastatic disease | | |
| Head and neck | Head and neck ¹ | 18-40 | 57 | 3,399 | 1.68 | 18.69 | White | 819 | 59,043 | 1.39 | 9.55 | Male | 780 | 54,314 | 7,862 | 1.44 | 9.92 | | |
| | | 41-60 | 395 | 29,942 | 1.32 | 8.73 | Black | 103 | 6,300 | 1.63 | 11.12 | Female | 334 | 23,296 | 3,405 | 1.43 | 9.81 | | |
| | | 61-80 | 522 | 36,216 | 1.44 | 9.53 | Hispanic | 99 | 6,062 | 1.63 | 12.04 | | | | | | | | |
| | | >80 | 96 | 8,053 | 1.19 | 10.00 | Asian or Pacific Islander | 80 | 5,093 | 1.57 | 10.99 | | | | | | | | |
| | | | | | | | American Indian/Alaska Native | 5 | 480 | 1.04 | 7.81 | | | | | | | | |
| | | | | | | | Unknown | 8 | 632 | 1.27 | 8.99 | | | | | | | | |
| | | | | | | | White | 380 | 57,307 | 0.66 | 19.84 | Male | 309 | 21,708 | 1,427 | 1.42 | 21.65 | | |
| | | | | | | | Black | 103 | 6,109 | 1.69 | 34.92 | Female | 370 | 66,648 | 1,920 | 0.56 | 19.27 | | |
| | | | | | | | Hispanic | 92 | 14,305 | 0.64 | 13.61 | | | | | | | | |
| | | | | | | | Asian or Pacific Islander | 100 | 9,179 | 1.09 | 23.75 | | | | | | | | |
| | | | | | | | American Indian/Alaska Native | 3 | 532 | 0.56 | 11.11 | | | | | | | | |
| | | Thyroid | Thyroid | 18-40 | 37 | 24,002 | 0.15 | 9.16 | White | 380 | 57,307 | 0.66 | 19.84 | Male | 309 | 21,708 | 1,427 | 1.42 | 21.65 |
| 41-60 | 186 | | | 39,558 | 0.47 | 19.79 | Black | 103 | 6,109 | 1.69 | 34.92 | Female | 370 | 66,648 | 1,920 | 0.56 | 19.27 | | |
| 61-80 | 370 | | | 22,434 | 1.65 | 24.25 | Hispanic | 92 | 14,305 | 0.64 | 13.61 | | | | | | | | |
| >80 | 86 | | | 2,362 | 3.64 | 18.03 | Asian or Pacific Islander | 100 | 9,179 | 1.09 | 23.75 | | | | | | | | |
| | | | | | | | American Indian/Alaska Native | 3 | 532 | 0.56 | 11.11 | | | | | | | | |
| | | | | | | | Unknown | 1 | 924 | 0.11 | 7.69 | | | | | | | | |
| Breast | Breast | | | 18-40 | 1,140 | 24,616 | 4.63 | 50.11 | White | 10,908 | 298,403 | 3.66 | 55.70 | Male | 210 | 3,414 | 335 | 6.15 | 62.69 |
| | | | | 41-60 | 6,294 | 176,055 | 3.58 | 52.34 | Black | 2,447 | 48,090 | 5.09 | 50.19 | Female | 16,051 | 432,933 | 29,981 | 3.71 | 53.54 |
| | | | | 61-80 | 7,022 | 194,444 | 3.61 | 56.07 | Hispanic | 1,707 | 48,576 | 3.51 | 48.72 | | | | | | |
| | | | | >80 | 1,805 | 41,232 | 4.38 | 51.69 | Asian or Pacific Islander | 1,067 | 36,476 | 2.93 | 51.37 | | | | | | |
| | | | | | | | | | American Indian/Alaska Native | 85 | 2,392 | 3.55 | 47.22 | | | | | | |
| | | | | | | | | | Unknown | 47 | 2,410 | 1.95 | 48.45 | | | | | | |
| | | Respiratory system | Small cell | 18-40 | 25 | 115 | 21.74 | 34.72 | White | 7,793 | 32,785 | 23.77 | 35.42 | Male | 5,103 | 19,710 | 13,736 | 25.89 | 37.15 |
| | | | | 41-60 | 2,320 | 9,373 | 24.75 | 35.73 | Black | 714 | 3,547 | 20.13 | 29.86 | Female | 4,120 | 20,059 | 12,950 | 20.54 | 31.81 |
| | | | | 61-80 | 6,070 | 25,894 | 23.44 | 35.34 | Hispanic | 399 | 1,823 | 21.89 | 32.28 | | | | | | |
| | | | | >80 | 808 | 4,387 | 18.42 | 27.45 | Asian or Pacific Islander | 271 | 1,348 | 20.10 | 30.08 | | | | | | |
| | | | | | | | | | American Indian/Alaska Native | 42 | 230 | 18.26 | 29.37 | | | | | | |
| | | | | | | | | | Unknown | 4 | 36 | 11.11 | 25.00 | | | | | | |
| Squamous cell carcinoma | 18-40 | | 32 | 441 | 7.26 | 19.05 | White | 5,869 | 71,748 | 8.18 | 22.49 | Male | 5,351 | 61,490 | 22,226 | 8.70 | 24.08 | | |
| | 41-60 | | 1,615 | 18,183 | 8.88 | 24.13 | Black | 1,107 | 11,761 | 9.41 | 25.89 | Female | 2,516 | 31,750 | 11,617 | 7.92 | 21.66 | | |
| | 61-80 | | 5,100 | 60,633 | 8.41 | 23.33 | Hispanic | 440 | 5,281 | 8.33 | 22.94 | | | | | | | | |
| | >80 | | 1,120 | 13,983 | 8.01 | 21.87 | Asian or Pacific Islander | 402 | 3,696 | 10.88 | 30.99 | | | | | | | | |
| | | | | | | | American Indian/Alaska Native | 41 | 556 | 7.37 | 21.35 | | | | | | | | |
| | | | | | | | Unknown | 8 | 198 | 4.04 | 11.76 | | | | | | | | |
| Adenocarcinoma | Adenocarcinoma | 18-40 | 345 | 1,109 | 31.11 | 44.92 | White | 21,226 | 107,687 | 19.71 | 37.07 | Male | 16,070 | 76,262 | 41,174 | 21.07 | 39.03 | | |
| | | 41-60 | 7,992 | 32,581 | 24.53 | 39.62 | Black | 3,373 | 16,920 | 19.93 | 33.42 | Female | 13,776 | 70,932 | 39,807 | 19.42 | 34.61 | | |
| | | 61-80 | 17,748 | 90,582 | 19.59 | 37.44 | Hispanic | 2,122 | 9,477 | 22.39 | 37.54 | | | | | | | | |
| | | >80 | 3,761 | 22,922 | 16.41 | 29.75 | Asian or Pacific Islander | 2,961 | 12,234 | 24.20 | 39.50 | | | | | | | | |
| | | | | | | | American Indian/Alaska Native | 133 | 626 | 21.25 | 35.75 | | | | | | | | |
| | | | | | | | Unknown | 41 | 280 | 14.64 | 36.94 | | | | | | | | |
| | Bronchioloalveolar adenocarcinoma | 18-40 | 3 | 29 | 10.34 | 27.27 | White | 123 | 3,383 | 3.64 | 16.97 | Male | 96 | 1,701 | 585 | 5.64 | 16.41 | | |
| | | 41-60 | 38 | 657 | 5.78 | 25.85 | Black | 23 | 380 | 6.05 | 21.10 | Female | 88 | 2,774 | 439 | 3.17 | 20.05 | | |
| | | 61-80 | 111 | 2,935 | 3.78 | 17.62 | Hispanic | 15 | 308 | 4.87 | 18.07 | | | | | | | | |
| | | >80 | 32 | 854 | 3.75 | 13.56 | Asian or Pacific Islander | 23 | 391 | 5.88 | 21.50 | | | | | | | | |
| | | | | | | | American Indian/Alaska Native | 0 | 8 | 0.00 | 0.00 | | | | | | | | |
| | | | | | | | Unknown | 0 | 5 | 0.00 | 0.00 | | | | | | | | |
| Non-small cell and other | Non-small cell and other | 18-40 | 30 | 102 | 29.41 | 38.96 | White | 3,297 | 15,419 | 21.38 | 34.00 | Male | 2,681 | 11,654 | 7,699 | 23.00 | 34.82 | | |
| | | 41-60 | 1,163 | 4,471 | 26.01 | 35.49 | Black | 522 | 2,733 | 19.10 | 29.03 | Female | 1,758 | 8,968 | 5,525 | 19.60 | 31.82 | | |
| | | 61-80 | 2,631 | 12,521 | 21.01 | 33.47 | Hispanic | 310 | 1,977 | 15.68 | 36.56 | | | | | | | | |
| | | >80 | 615 | 3,528 | 17.43 | 30.60 | Asian or Pacific Islander | 291 | 1,119 | 26.01 | 36.28 | | | | | | | | |
| | | | | | | | American Indian/Alaska Native | 14 | 119 | 11.76 | 22.58 | | | | | | | | |
| | | | | | | | Unknown | 5 | 35 | 14.29 | 27.78 | | | | | | | | |
| | Digestive system | Esophagus | 18-40 | 29 | 279 | 10.39 | 21.80 | White | 1,626 | 19,952 | 8.15 | 21.28 | Male | 1,788 | 20,367 | 8,211 | 6.78 | 21.78 | |
| | | | 41-60 | 703 | 6,829 | 10.29 | 22.55 | Black | 197 | 2,584 | 7.62 | 19.13 | Female | 287 | 5,588 | 1,749 | 5.14 | 16.41 | |
| | | | 61-80 | 1,142 | 15,024 | 7.60 | 20.19 | Hispanic | 157 | 2,009 | 7.81 | 19.48 | | | | | | | |
| | | | >80 | 201 | 3,823 | 5.26 | 18.31 | Asian or Pacific Islander | 73 | 1,181 | 6.18 | 16.74 | | | | | | | |
| | | | | | | | | American Indian/Alaska Native | 22 | 165 | 13.33 | 28.95 | | | | | | | |
| | | | | | | | | Unknown | 0 | 64 | 0.00 | 0.00 | | | | | | | |
| Gastric | | 18-40 | 130 | 1,696 | 7.67 | 15.31 | White | 1,114 | 23,122 | 4.82 | 13.51 | Male | 1,283 | 26,580 | 10,021 | 4.83 | 12.80 | | |
| | | 41-60 | 674 | 11,615 | 5.80 | 14.09 | Black | 198 | 5,931 | 3.34 | 9.56 | Female | 664 | 16,990 | 5,504 | 3.91 | 12.06 | | |
| | | 61-80 | 936 | 22,168 | 4.22 | 12.25 | Hispanic | 374 | 8,099 | 4.62 | 11.84 | | | | | | | | |
| | | >80 | 207 | 8,091 | 2.56 | 9.19 | Asian or Pacific Islander | 239 | 5,889 | 4.06 | 12.71 | | | | | | | | |
| | | | | | | | American Indian/Alaska Native | 20 | 371 | 5.39 | 13.42 | | | | | | | | |
| | | | | | | | Unknown | 2 | 158 | 1.27 | 9.09 | | | | | | | | |
| Hepatobiliary | Hepatobiliary | 18-40 | 44 | 1,085 | 4.06 | 12.68 | White | 1,816 | 38,991 | 4.66 | 19.67 | Male | 2,365 | 47,281 | 9,859 | 5.00 | 23.99 | | |
| | | 41-60 | 1,104 | 22,942 | 4.81 | 21.48 | Black | 441 | 8,931 | 4.94 | 20.89 | Female | 821 | 24,734 | 6,595 | 3.32 | 12.45 | | |
| | | 61-80 | 1,735 | 38,658 | 4.49 | 19.53 | Hispanic | 544 | 13,552 | 4.01 | 18.39 | | | | | | | | |
| | | >80 | 303 | 9,330 | 3.25 | 14.54 | Asian or Pacific Islander | 345 | 9,585 | 3.60 | 17.48 | | | | | | | | |
| | | | | | | | American Indian/Alaska Native | 37 | 773 | 4.79 | 23.13 | | | | | | | | |
| | | | | | | | Unknown | 3 | 183 | 1.64 | 15.00 | | | | | | | | |
| | Pancreatic | 18-40 | 41 | 1,119 | 3.66 | 8.69 | White | 1,947 | 51,673 | 3.77 | 7.18 | Male | 1,695 | 38,321 | 20,973 | 4.42 | 8.08 | | |
| | | 41-60 | 727 | 16,856 | 4.31 | 7.77 | Black | 327 | 9,028 | 3.62 | 6.41 | Female | 1,176 | 36,339 | 18,562 | 3.24 | 6.34 | | |
| | | 61-80 | 1,691 | 41,976 | 4.03 | 7.49 | Hispanic | 301 | 7,957 | 3.78 | 7.00 | | | | | | | | |
| | | >80 | 376 | 14,709 | 2.56 | 5.27 | Asian or Pacific Islander | 238 | 5,454 | 4.36 | 8.66 | | | | | | | | |
| | | | | | | | American Indian/Alaska Native | 19 | 406 | 4.68 | 8.60 | | | | | | | | |
| | | | | | | | Unknown | 3 | 142 | 2.11 | 5.26 | | | | | | | | |
| Colorectal | Colorectal | 18-40 | 131 | 9,175 | 1.43 | 5.76 | White | 1,969 | 166,744 | 1.18 | 5.76 | Male | 1,878 | 130,273 | 27,775 | 1.44 | 6.76 | | |
| | | 41-60 | 1,023 | 76,643 | 1.33 | 5.77 | Black | 468 | 30,329 | 1.54 | 6.18 | Female | 1,207 | 119,000 | 24,536 | 1.01 | 4.92 | | |
| | | 61-80 | 1,459 | 117,593 | 1.24 | 6.15 | Hispanic | 371 | 28,276 | 1.31 | 6.13 | | | | | | | | |
| | | >80 | 472 | 45,862 | 1.03 | 5.49 | Asian or Pacific Islander | 244 | 20,419 | 1.19 | 6.08 | | | | | | | | |
| | | | | | | | American Indian/Alaska Native | 27 | 1,850 | 1.46 | 6.35 | | | | | | | | |
| | | | | | | | Unknown | 6 | 1,654 | 0.36 | 8.00 | | | | | | | | |
| | Anal | 18-40 | 2 | 371 | 0.54 | 3.92 | White | 84 | 9,288 | 0.91 | 7.25 | Male | 53 | 4,481 | 524 | 1.18 | 10.11 | | |
| | | 41-60 | 52 | 5,328 | 0.98 | 7.69 | Black | 17 | 1,344 | 1.26 | 9.24 | Female | 68 | 7,669 | 1,060 | 0.89 | 6.42 | | |
| | | 61-80 | 56 | 5,1 | | | | | | | | | | | | | | | |

Table S2 Median survival of patients with bone metastases by age, race, and gender

| Site | Sub-site | Age | | | Race | Race | | Gender | Gender | | |
|---------------|----------------------------|-----------------------------------|---|---|-------------------------------|---|---|---------------|---|---|---------------|
| | | Age category in years | Number of patients with bone metastases | Median survival in months (interquartile range) | | Number of patients with bone metastases | Median survival in months (interquartile range) | | Number of patients with bone metastases | Median survival in months (interquartile range) | |
| Head and neck | Head and neck ¹ | 18-40 | 57 | 15 [8-32] | White | 819 | 8 [3-16] | Male | 780 | 8 [3-18] | |
| | | 41-60 | 395 | 9 [3-21] | Black | 103 | 8 [3-18] | Female | 334 | 8 [3-15] | |
| | | 61-80 | 522 | 7 [3-16] | Hispanic | 99 | 8 [3-20] | | | | |
| | | >80 | 96 | 4 [1-10] | Asian or Pacific Islander | 80 | 15 [8-35] | | | | |
| | | | | | American Indian/Alaska Native | 5 | 10 [5-15] | | | | |
| | | | Unknown | 8 | 11 [3-16] | | | | | | |
| Thyroid | Thyroid | 18-40 | 37 | 52 [9-NR] | White | 380 | 21 [4-82] | Male | | 22 [4-82] | |
| | | 41-60 | 186 | 66 [7-NR] | Black | 103 | 27 [3-60] | Female | | 23 [3-NR] | |
| | | 61-80 | 370 | 22 [4-NR] | Hispanic | 92 | 21 [3-64] | | | | |
| | | >80 | 86 | 6 [2-23] | Asian or Pacific Islander | 100 | 49 [9-NR] | | | | |
| | | | | | American Indian/Alaska Native | 3 | 2 [NR] | | | | |
| | | | Unknown | 1 | 5 [NR] | | | | | | |
| Breast | Breast | 18-40 | 1,140 | 42 [20-72] | White | 10,908 | 28 [8-59] | Male | | 23 [8-54] | |
| | | 41-60 | 6,294 | 32 [13-66] | Black | 2,447 | 20 [6-43] | Female | | 27 [8-57] | |
| | | 61-80 | 7,022 | 25 [6-53] | Hispanic | 1,707 | 32 [12-63] | | | | |
| | | >80 | 1,805 | 12 [2-32] | Asian or Pacific Islander | 1,067 | 31 [12-62] | | | | |
| | | | | | American Indian/Alaska Native | 85 | 34 [12-NR] | | | | |
| | | | Unknown | 47 | NR [22-NR] | | | | | | |
| Lung | Small cell | 18-40 | 25 | 8 [4-10] | White | 7,793 | 5 [1-10] | Male | 5103 | 5 [1-10] | |
| | | 41-60 | 2,320 | 7 [2-11] | Black | 714 | 8.0 [2.0-16.0] | Female | 4,120 | 6 [1-10] | |
| | | 61-80 | 6,070 | 5 [1-10] | Hispanic | 399 | 4 [1-10] | | | | |
| | | >80 | 808 | 2 [0-6] | Asian or Pacific Islander | 271 | 6 [2-10] | | | | |
| | | | | | American Indian/Alaska Native | 42 | 3 [1-9] | | | | |
| | | | | Unknown | 4 | 18 [5-18] | | | | | |
| | | Squamous cell carcinoma | 18-40 | 32 | 8 [2.0-15.0] | White | 5,869 | 3.0 [1.0-7.0] | Male | 5,351 | 3.0 [1.0-7.0] |
| | 41-60 | | 1,615 | 4.0 [2.0-9.0] | Black | 1,107 | 3.0 [1.0-8.0] | Female | 2,516 | 3.0 [1.0-7.0] | |
| | 61-80 | | 5,100 | 3.0 [1.0-7.0] | Hispanic | 440 | 3.0 [1.0-9.0] | | | | |
| | >80 | | 1,120 | 2.0 [1.0-5.0] | Asian or Pacific Islander | 402 | 4.0 [1.0-9.0] | | | | |
| | | | | | American Indian/Alaska Native | 41 | 4.0 [1.0-11.0] | | | | |
| | | | | Unknown | 8 | 2.0 [1.0-9.0] | | | | | |
| | | Adenocarcinoma | 18-40 | 3 | 14 [5-29] | White | 21,226 | 4 [1-12] | Male | 16,070 | 4 [1-11] |
| | 41-60 | | 38 | 6 [2-16] | Black | 3,373 | 4 [1-11] | Female | 13,776 | 5 [2-15] | |
| | 61-80 | | 111 | 4 [1-12] | Hispanic | 2,122 | 6 [2-15] | | | | |
| | >80 | | 32 | 3 [1-8] | Asian or Pacific Islander | 2,961 | 11 [3-25] | | | | |
| | | | | | American Indian/Alaska Native | 133 | 5 [1-10] | | | | |
| | | | | Unknown | 41 | 13 [2-32] | | | | | |
| | | Bronchioloalveolar adenocarcinoma | 18-40 | - | 22 [4-38] | White | 92 | 6 [2-16] | Male | 96 | 7 [2-19] |
| | 41-60 | | 50 | 10 [5-21] | Black | 20 | 5 [1-16] | Female | 88 | 9 [3-2] | |
| 61-80 | 84 | | 7 [2-21] | Hispanic | 11 | 11 [4-21] | | | | | |
| >80 | 13 | | 6 [2-12] | Asian or Pacific Islander | 23 | 22 [9-39] | | | | | |
| | | | | American Indian/Alaska Native | 1 | NA | | | | | |
| | | | Unknown | 0 | NA | | | | | | |
| | Non-small cell and other | 18-40 | 30 | 7 [5-15] | White | 3,297 | 3 [1-7] | Male | 2,681 | 3 [1-7] | |
| 41-60 | | 1,163 | 4 [1-9] | Black | 522 | 3 [1-7] | Female | 1,728 | 3 [1-9] | | |
| 61-80 | | 2,631 | 3 [1-8] | Hispanic | 310 | 3 [1-10] | | | | | |
| >80 | | 615 | 2 [1-5] | Asian or Pacific Islander | 291 | 4 [1-15] | | | | | |
| | | | | American Indian/Alaska Native | 14 | 2 [1-5] | | | | | |
| | | | Unknown | 5 | 2 [1-5] | | | | | | |
| GI | Esophagus | 18-40 | 29 | 9 [2-31] | White | 198 | 11 [4-37] | Male | 287 | 11 [4-35] | |
| | | 41-60 | 703 | 13 [4-38] | Black | 14 | 12 [5-33] | Female | 1,788 | 11 [3-44] | |
| | | 61-80 | 1,142 | 11 [4-38] | Hispanic | 16 | 13 [4-43] | | | | |
| | | >80 | 201 | 11 [4-32] | Asian or Pacific Islander | 9 | 13 [4-43] | | | | |
| | | | | | American Indian/Alaska Native | 1 | 8 [4-19] | | | | |
| | | | | Unknown | 0 | NA | | | | | |
| | | Gastric | 18-40 | 130 | 5 [1-10] | White | 1,114 | 4 [1-9] | Male | 1,283 | 3 [1-8] |
| | 41-60 | | 674 | 4 [1-9] | Black | 198 | 3 [1-7] | Female | 664 | 3 [1-8] | |
| | 61-80 | | 936 | 3 [1-9] | Hispanic | 374 | 3 [1-8] | | | | |
| | >80 | | 207 | 2 [0-5] | Asian or Pacific Islander | 239 | 3 [1-8] | | | | |
| | | | | | American Indian/Alaska Native | 20 | 5 [1-6] | | | | |
| | | | | Unknown | 2 | NA | | | | | |
| | | Hepatobiliary | 18-40 | 44 | 7 [3-13] | White | 1,816 | 3 [1-8] | Male | 2,365 | 3 [1-7] |
| | 41-60 | | 1,104 | 3 [1-7] | Black | 441 | 3 [1-7] | Female | 821 | 3 [1-8] | |
| | 61-80 | | 1,735 | 3 [1-7] | Hispanic | 544 | 3 [1-8] | | | | |
| | >80 | | 303 | 2 [0-5] | Asian or Pacific Islander | 345 | 3 [1-7] | | | | |
| | | | | | American Indian/Alaska Native | 37 | 3 [1-9] | | | | |
| | | | | Unknown | 3 | 5 [1-5] | | | | | |
| | | Pancreatic | 18-40 | 41 | 8 [2-20] | White | 51,673 | 2 [1-6] | Male | 1,695 | 2 [1-6] |
| | 41-60 | | 727 | 3 [1-8] | Black | 9,028 | 2 [1-6] | Female | 1,176 | 2 [1-6] | |
| 61-80 | 1,691 | | 2 [1-6] | Hispanic | 7,957 | 2 [1-8] | | | | | |
| >80 | 376 | | 1 [0-3] | Asian or Pacific Islander | 5,454 | 2 [1-6] | | | | | |
| | | | | American Indian/Alaska Native | 406 | 1 [0-5] | | | | | |
| | | | Unknown | 142 | 0 [0-1] | | | | | | |
| | Colorectal | 18-40 | 131 | 10 [3-23] | White | 166,744 | 5 [1-14] | Male | 1,878 | 5 [1-15] | |
| 41-60 | | 1,023 | 9 [3-20] | Black | 30,329 | 4 [2-15] | Female | 1,207 | 5 [1-14] | | |
| 61-80 | | 1,459 | 4 [1-13] | Hispanic | 28,276 | 5 [2-18] | | | | | |
| >80 | | 472 | 2 [0-5] | Asian or Pacific Islander | 20,419 | 7 [2-19] | | | | | |
| | | | | American Indian/Alaska Native | 1,850 | 6 [4-9] | | | | | |
| | | | Unknown | 1,654 | 14 [2-14] | | | | | | |
| | Anal | 18-40 | 2 | NA | White | 9,268 | 10 [5-27] | Male | 53 | 8 [4-22] | |
| 41-60 | | 52 | 14 [5-46] | Black | 1,344 | 6 [5-22] | Female | 68 | 14 [4-27] | | |
| 61-80 | | 56 | 9 [4-24] | Hispanic | 1,097 | 4 [2-NR] | | | | | |
| >80 | | 11 | 3 [1-8] | Asian or Pacific Islander | 311 | 5 [1-6] | | | | | |
| | | | | American Indian/Alaska Native | 65 | NA | | | | | |
| | | | Unknown | 65 | NA | | | | | | |
| | Other GI | 18-40 | 21 | 4 [1-11] | White | 15,935 | 3 [1-8] | Male | 344 | 3 [1-10] | |
| 41-60 | | 237 | 2 [1-8] | Black | 3,324 | 2 [0-10] | Female | 512 | 2 [1-7] | | |
| 61-80 | | 457 | 3 [1-9] | Hispanic | 2,624 | 2 [0-6] | | | | | |
| >80 | | 141 | 2 [0-5] | Asian or Pacific Islander | 1,379 | 2 [1-10] | | | | | |
| | | | | American Indian/Alaska Native | 142 | 4 [1-6] | | | | | |
| | | | Unknown | 109 | 2 [2-NR] | | | | | | |
| GU | Renal | 18-40 | 128 | 10 [4-24] | White | 68,184 | 6 [2-17] | Male | 3,820 | 6 [2-18] | |
| | | 41-60 | 1,740 | 8 [3-26] | Black | 12,112 | 5 [2-14] | Female | 1,783 | 5 [2-15] | |
| | | 61-80 | 2,976 | 6 [2-17] | Hispanic | 14,206 | 7 [2-19] | | | | |
| | | >80 | 759 | 3 [1-7] | Asian or Pacific Islander | 5,234 | 6 [2-20] | | | | |
| | | | | | American Indian/Alaska Native | 885 | 6 [2-12] | | | | |
| | | | | Unknown | 500 | 5 [5-50] | | | | | |
| | | Bladder | 18-40 | 15 | 8 [4-10] | White | 102,014 | 4 [1-10] | Male | 1,390 | 4 [1-10] |
| | 41-60 | | 385 | 5 [2-11] | Black | 7,255 | 4 [2-8] | Female | 450 | 3 [1-8] | |
| | 61-80 | | 1,029 | 4 [1-11] | Hispanic | 7,846 | 4 [1-4] | | | | |
| | >80 | | 411 | 2 [1-6] | Asian or Pacific Islander | 5,196 | 5 [1-10] | | | | |
| | | | | | American Indian/Alaska Native | 415 | 1 [1-5] | | | | |
| | | | | Unknown | 1,553 | 5 [NR] | | | | | |
| | | Prostate | 18-40 | 14 | 22 [13-38] | White | 234,522 | 25 [10-53] | Male | 19,750 | 25 [11-55] |
| | 41-60 | | 3,321 | 34 [17-72] | Black | 53,642 | 25 [11-55] | Female | 0 | NA | |
| | 61-80 | | 11,230 | 29 [12-65] | Hispanic | 32,440 | 24 [11-61] | | | | |
| | >80 | | 5,185 | 15 [5-33] | Asian or Pacific Islander | 16,142 | 34 [13-NR] | | | | |
| | | | | | American Indian/Alaska Native | 1,316 | 26 [10-55] | | | | |
| | | | | Unknown | 8,782 | NR | | | | | |
| | | Testicular | 18-40 | 87 | NR [8-NR] | White | 11,001 | 21.0 [4.5-NR] | Male | 143 | NR [7-NR] |
| | 41-60 | | 42 | 32 [4-NR] | Black | 506 | NA | Female | 0 | NA | |
| 61-80 | 14 | | 8 [3-NR] | Hispanic | 1,959 | NR [NR-NR] | | | | | |
| >80 | - | | NA | Asian or Pacific Islander | 712 | NR [14.0-NR] | | | | | |
| | | | | American Indian/Alaska Native | 180 | 14.0 [NR] | | | | | |
| | | | Unknown | 303 | NR | | | | | | |
| | Other GU | 18-40 | 6 | 5 [5-18] | White | 6,130 | 4 [1-9] | Male | 199 | 4 [1-9] | |
| 41-60 | | 40 | 7 [2-14] | Black | 703 | 5 [3-9] | Female | 88 | 4 [1-10] | | |
| 61-80 | | 153 | 5 [1-9] | Hispanic | 977 | 4 [1-9] | | | | | |
| >80 | | 88 | 2 [1-7] | Asian or Pacific Islander | 549 | 5 [2-14] | | | | | |
| | | | | American Indian/Alaska Native | 41 | 7 [7-9] | | | | | |
| | | | Unknown | 67 | 4 [1-9] | | | | | | |
| GYN | Ovarian | 18-40 | 25 | 5 [2-9] | White | 25,567 | 4 [1-15] | Male | 0 | NA | |
| | | 41-60 | 121 | 7 [2-19] | Black | 3,270 | 7 [2-36] | Female | 422 | 5 [1-17] | |
| | | 61-80 | 202 | 5 [1-23] | Hispanic | 5,073 | 4 [1-10] | | | | |
| | | >80 | 74 | 2 [0-7] | Asian or Pacific Islander | 3,209 | 7 [1-14] | | | | |
| | | | | | American Indian/Alaska Native | 220 | 2 [NR-NR] | | | | |
| | | | | Unknown | 129 | NA | | | | | |
| | | Endometrial | 18-40 | 17 | 5 [5-10] | White | 12,015 | 6 [2-17] | Male | 0 | NA |
| | 41-60 | | 320 | 8 [2-20] | Black | 3,084 | 4 [1-12] | Female | 847 | 6 [2-15] | |
| | 61-80 | | 436 | 6 [1-15] | Hispanic | 5,164 | 6 [1-15] | | | | |
| | >80 | | 74 | 3 [1-10] | Asian or Pacific Islander | 2,124 | 9 [3-28] | | | | |
| | | | | | American Indian/Alaska Native | 208 | 10 [9-20] | | | | |
| | | | | Unknown | 179 | NA | | | | | |
| | | Cervical | 18-40 | 75 | 8 [3-15] | White | 120 | 6 [2-16] | Male | 0 | NA |
| | 41-60 | | 163 | 7 [3-18] | Black | 1,347 | 5 [3-12] | Female | 558 | 6 [2-15] | |
| | 61-80 | | 190 | 5 [2-13] | Hispanic | 1,522 | 6 [2-14] | | | | |
| | >80 | | 30 | 3 [1-7] | Asian or Pacific Islander | 751 | 12 [4-23] | | | | |
| | | | | | American Indian/Alaska Native | 104 | 1 [NR-13] | | | | |
| | | | | Unknown | 112 | NR [NR-NR] | | | | | |
| | | Other GYN | 18-40 | 7 | 8 [3-NR] | White | 24,834 | 5 [2-17] | Male | 0 | NA |
| | 41-60 | | 49 | 9 [3-29] | | | | | | | |