



BONE METASTASES FROM SOLID TUMOURS

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ABSTRACT

The skeleton is one of the most common sites for metastasis, and tumors arising from the breast, prostate and lung possess an increased propensity to spread to this site. Bone metastasis distal to the elbow and knee joint are extremely rare. Metastasis could be either solitary or multiple depending on the primary cancer. Solitary metastasis is more common with breast cancer whereas multiple metastases are more common with prostate cancer.

KEYWORDS : Metastasis, Bone, Breast, Prostate, Lung

Introduction

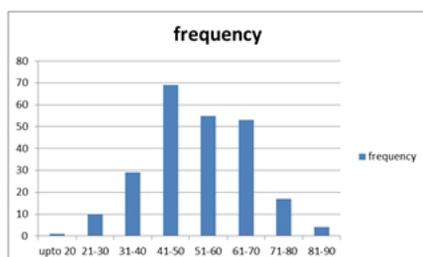
Bone metastasis is a common presentation of distant relapse from many types of solid cancers, especially those arising in the breast, prostate, and lung^{1,2}. The prevalence of bone metastases is difficult to quantify, as the incidence is affected by the sensitivity of diagnostic tools and the duration of patient survival. The bone is the third most common organ affected by metastasis, after the lung and liver. The distant metastasis, especially those involving bone, increase mortality rate, shorten patient survival and compromise quality of life³⁻⁶. Skeletal-related events that are due to bone metastasis can include pain, impaired mobility, hypercalcemia, increased incidence of pathologic fracture and spinal cord compression. Bone metastasis also occurs in other cancer types, including carcinomas of the kidney, melanoma and bladder^{7,8}. The spine is infamously known to be the most common site of skeletal metastasis⁹. Bone lesions are found more commonly within the axial skeletal in comparison to the appendicular skeleton¹⁰. Although any skeletal bone may be involved with metastatic disease, the vertebral body is most commonly associated with metastatic disease; whereas bone metastases distal to the elbow and knee are considered rare¹¹⁻¹⁴. According to Katagiri et al^{15,16}, lungs, breasts, prostate and liver were the most common sources of solitary bone metastasis, while in a study by Shih et al¹⁷, the most common primary sites with solitary bone metastasis were the prostate, thyroid, kidney, lungs and liver.

Material & Methods

Two hundred and thirty eight patients with metastatic bone disease from various primaries excluding haematological malignancies and patients with insufficient data in medical records, who reported at the Department of Radiotherapy, Chittaranjan National Cancer Institute, Kolkata, India during the time frame January 1st 2013 – December 31st 2016 were included in our study. Information retrospectively collected on these patients included patient age, gender, primary, site of bone metastasis and number of bone metastases. Patients with known primary cancer and radiologically proved bone metastasis were included in the study. The presence of bone metastasis in all the patients was proved by histopathological examination.

Analysis & Results

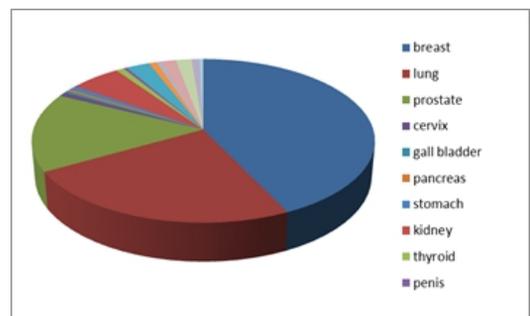
Figure 1: Age Group



Age group (years)	upto 20	21-30	31-40	41-50	51-60	61-70	71-80	81-90
Frequency	1	10	29	69	55	53	17	4
Median Age (years)	Breast	Prostate	Lung	Kidney	Urinary Bladder			
	45	68	58	51	67			

Figure 2: Primary Cancer

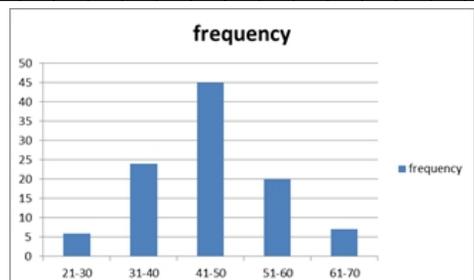
A total of 238 patients had metastatic bone disease, with the highest incidence at the age of 41–50 years. Most of the patients in the study were aged 41–70 years (HYPERLINK "https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4293965/figure/F1/" "figure" Figure 1). The youngest was a 14 year old female patient with nasopharyngeal carcinoma.



The commonest primary cancer was breast (42.9%), followed by lung (23.9%), prostate (15.5%) and renal cell carcinoma (5.5%).

Figure 3: Ca.Breast with bone metastases – Age Group

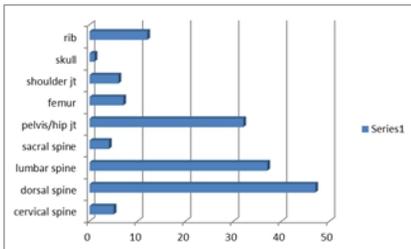
Breast	Lung	Prostate	Cervix	Gall Bladder	Pancreas	Stomach	Kidney	Thyroid	Penis	Urinary Bladder	Parotid	Submandibular Gland	Nasopharynx	Rectum	Anal Canal	Ureter
102	57	37	2	1	1	2	13	2	1	6	2	1	4	4	2	1



age group	21-30	31-40	41-50	51-60	61-70
frequency	6	24	45	20	7

Among the 102 patients affected with breast cancer, most common age group affected with bone metastasis was 41-50 years (44.1%) followed by 31-40 years (23.5%)

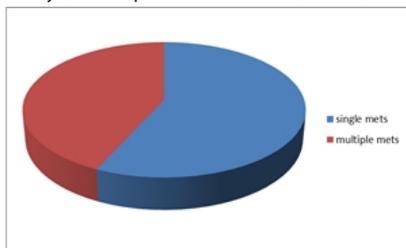
Figure 4: Site of bone metastases from Ca.Breast



Cervical spine	Dorsal spine	Lumbar spine	Sacral spine	Pelvis/Hip joint	Femur	Shoulder joint	Skull	Rib
5	47	37	4	32	7	6	1	12

The most common site affected with bone metastasis from breast cancer was the dorsal spine followed by lumbar spine and pelvis

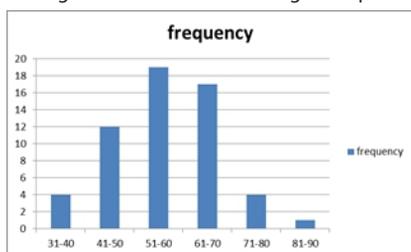
Figure 5: Solitary v/s Multiple bone metastases from Ca.Breast



single metastasis	multiple metastases
58	44

In our study, the incidence of solitary bone metastasis (58) from breast cancer was higher when compared with multiple bone metastases (44).

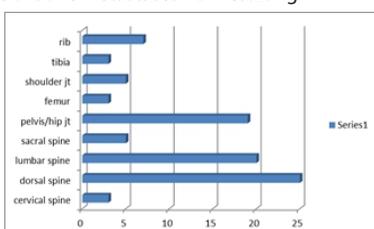
Figure 6: Ca.Lung with bone metastases – Age Group



age group	31-40	41-50	51-60	61-70	71-80	81-90
Frequency	4	12	19	17	4	1

Among the 57 patients affected with lung cancer, most common age group affected with bone metastasis was 51-60 years (33.3%) followed by 61-70 years (29.8%)

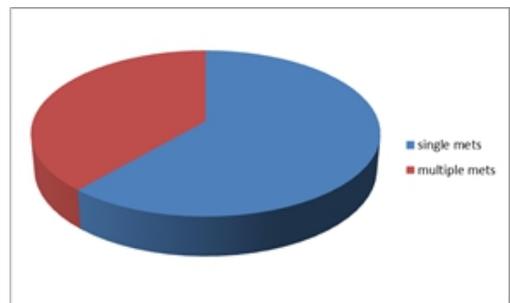
Figure 7: Site of bone metastases from Ca.Lung



cervical spine	dorsal spine	lumbar spine	sacral spine	pelvis/hip joint	Femur	shoulder joint	Tibia	Rib
3	25	20	5	19	3	5	3	7

Most common site affected with bone metastasis from lung cancer was the dorsal spine followed by lumbar spine and pelvis. Although rare, 3 patients reported with tibial metastasis.

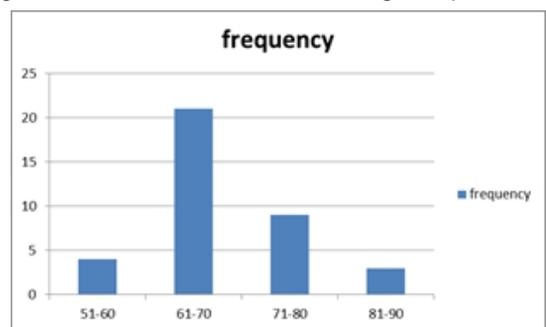
Figure 8: Solitary v/s Multiple bone metastases from Ca.Lung



Single metastases	Multiple metastases
35	22

The incidence of solitary bone metastasis (35) from lung cancer was higher when compared with multiple bone metastases (22).

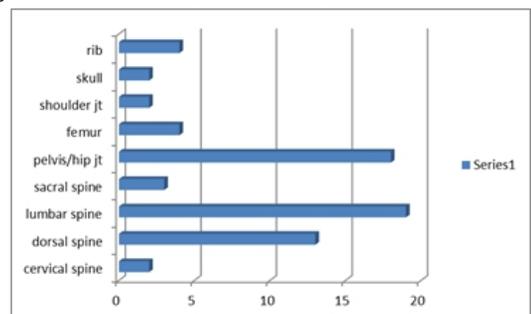
Figure 9: Ca.Prostate with bone metastases – Age Group



age group	51-60	61-70	71-80	81-90
frequency	4	21	9	3

Among the 37 patients affected with prostate cancer, most common age group affected with bone metastasis was 61-70 years (56.8%) followed by 71-80 years (24.3%).

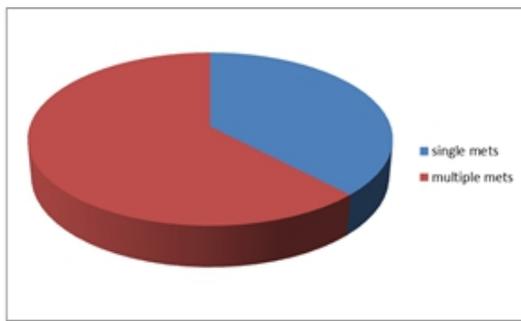
Figure 10: Site of bone metastases from Ca.Prostate



cervical spine	dorsal spine	lumbar spine	sacral spine	pelvis/hip joint	femur	shoulder joint	skull	rib
2	13	19	3	18	4	2	2	4

The most common site affected with bone metastasis from prostate cancer was the lumbar spine followed by pelvis and dorsal spine.

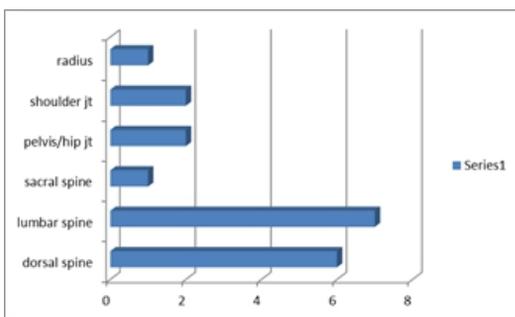
Figure 11: Solitary v/s Multiple metastases from Ca.Prostate



Single metastasis	Multiple metastases
14	23

The incidence of multiple bone metastases (23) from prostate cancer was higher when compared with solitary bone metastasis (14).

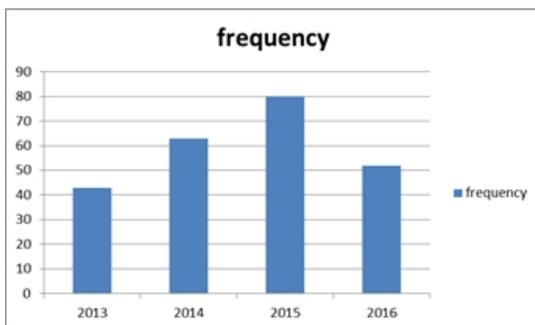
Figure 12: Site of bone metastases from Renal cell carcinoma



dorsal spine	lumbar spine	sacral spine	pelvis/hip joint	shoulder joint	Radius
6	7	1	2	2	1

The most common site affected with bone metastasis from renal cancer was the lumbar spine followed by dorsal spine. Although rare, one case reported with radial metastasis.

Figure 13: Year wise incidence of bone metastases



Year	Frequency
2013	43
2014	63
2015	80
2016	52

Frequency of bone metastasis was the highest in the year of 2015 followed by 2014, 2016 and 2013.

Discussion

Recently, there has been an increasing trend in the incidence of patients with metastatic bone disease. This could be attributed to longer duration of survival due to advancements in cancer treatment, greater awareness among patients, and better detection

of metastatic disease. The skeletal system being the most commonly affected organ in metastatic disease, is also known to be the site of metastasis that incurs the highest morbidity⁵. According to an extensive autopsy study by Berrettoni and Carter¹⁸, the individual tendency to metastasize to bone was 84% for prostate cancer, 84% for breast cancer, 50% for thyroid cancer, 44% for lung cancer, and 37% for renal cancer. Coleman stated that close to 80% of advanced breast and prostate cancer patients would eventually develop skeletal metastases⁷. Similarly, an autopsy study by Harrington¹⁹ reported high incidences of bone metastasis in breast and prostate cancers (84%) and much lower incidences in other primary cancers such thyroid (50%), lung (44%) and renal (37%) cancers. This could be due to the slow progression of breast and prostate cancers, leading to greater chances for the development of metastasis. Metastasis distal to the elbow and knee are rare. Tibia is the most common site when the metastasis is distal to the knee joint¹⁰. Barnes et al²⁰ concluded that the incidence to distal bone was most commonly associated with breast and lung primaries (23%) followed by prostate (19%).

1. Breast Cancer:

Breast cancer is the most common type of cancer in women, worldwide. Most common site to which breast cancer metastasizes is the bone²¹. Borst et al²² reported that in their series of 2605 breast tumors, lobular carcinoma accounted for 14% and ductal carcinoma for 86% of bone metastases. In our study most common site affected with bone metastasis from breast cancer was the dorsal spine followed by lumbar spine and pelvis, although the histological type of breast cancer was not taken into account. The incidence of solitary bone metastasis (56.9%) was higher when compared with multiple bone metastases (43.1%). Three male breast cancer patients with bone metastasis were also reported in the present study.

2. Lung Cancer:

Jaukovic et al²³ reported that 57 (57%) of their 100 patients with lung cancer metastasized to bone but only 6 of these 57 patients had a solitary metastasis. Tsuya et al²⁴ reported a rate of 30.4% skeletal metastases in 259 patients with lung cancer. In our study, among the 57 patients presented with bone metastasis from primary lung cancer the incidence of solitary bone metastasis (61.4%) was higher when compared with multiple bone metastases (38.6%). Most common sites affected were the dorsal spine followed by lumbar spine and pelvis. Although rare, 3 patients were reported with tibial metastasis.

3. Prostate Cancer:

Bone metastasis is a hallmark of advanced prostate cancer. The tumour spreads via the venous plexus, particularly to the lumbar spine and pelvis. An extensive autopsy study by Berrettoni and Carter stated an 84% chance of bone metastasis from prostate cancer¹⁸. In our study, the most common site affected was the lumbar spine followed by pelvis and dorsal spine. The incidence of multiple bone metastases (62.2%) from prostate cancer were higher when compared with solitary bone metastasis (37.8%).

4. Carcinoma of Kidney:

The most common site for metastasis from Renal Cell Carcinoma is the lung (50%), followed by the skeleton (20% to 50%)^{25,26}. About one-third of patients with metastatic kidney or bladder cancer and the majority of patients with castration resistant prostate cancer develop bone metastases^{27,28}. Shvarts et al²⁹ reported bone metastases in 14% of their 1357 patients with renal cell carcinoma. In our study, we noticed that the most common site affected with bone metastasis from renal cancer was the lumbar spine followed by dorsal spine. Solitary metastatic renal cell carcinoma to the radius is uncommon^{30,31}. The only case who reported with radial metastasis was included in our study.

5. Stomach Cancer:

Bone metastases from gastric cancer are rare³², with an incidence of

only 13.4% in autopsy specimens³³. The mechanism of bone metastasis in gastric carcinoma has been investigated by various authors, Lehnert et al³⁴ suggested that the high percentage of haematogenous metastases in recurrent early gastric cancer may be associated with the rich vascularity of the gastric mucosa. Batson et al³⁵ reported that metastasis to the spine from the stomach may occur through the paravertebral venous plexus because the intra-abdominal pressure is raised. In our study, only 2 cases were reported with bone metastasis from gastric cancer, reflecting the rarity of the incidence.

6. Urinary bladder Cancer:

Urothelial carcinoma of the bladder, the commonest histologic type, metastasizes to lymph nodes, liver, lung, bone, and adrenal gland³⁶. Taher et al³⁷ found that in muscle invasive bladder cancer the cumulative 3 year incidence of bone metastases in the non-metastatic patients after treatment mounted to 19.4 ± 4.4%. The authors found that, exactly like the breast and the prostate, the urinary bladder accounted for 6% of the solitary bone metastases. Witjes et al reported that 30 – 40% of patients with primary bladder cancer metastasize to bone^{38,39}. In our study, 2.5% among all the cases affected with metastatic bone disease was secondary to urinary bladder carcinoma.

7. Colorectal Cancer:

In an autopsy study by Katoh et al⁴⁰, 23.7% of patients with primary colorectal cancer were detected with bone metastases. Kanthan et al⁴¹ reported that solitary skeletal metastasis from a primary colon carcinoma is rare, with an incidence of 1.1%. In our study, bone metastases following carcinoma rectum accounted to 1.7%.

8. Nasopharyngeal Cancer:

The skeletal system is the most common site of distant metastases from nasopharyngeal carcinoma. The patients who developed skeletal metastases were significantly younger than those without skeletal metastases. The pattern of skeletal involvement conforms to the general pattern, the spine and pelvis being the common sites⁴². In our study, 4 cases of bone metastases were secondary to nasopharyngeal cancer. The youngest patient with bone metastasis was 14 years of age and was infact the youngest among all the cases.

9. Gall Bladder Cancer:

The incidence of bone metastasis in carcinoma gall bladder is rare⁴³⁻⁴⁵. In our study, only one case was recorded with bone metastasis from carcinoma gall bladder. Metastases was to Dorso-Lumbar spine.

10. Thyroid Cancer:

The bone is the 2nd most common site of systemic metastasis from thyroid carcinoma after lung^{46,47}. The overall incidence⁴⁸⁻⁵⁰ reported ranges from 1% to more than 40%. In our study, 2 cases were reported with bone metastases. Involved sites were lumbar and sacral spine.

11. Cervical Cancer:

The most common site of bone metastasis was lumbar vertebra, secondary to cervical cancer^{51,52}. Bone metastases have been reported in 1.1% patients with cervical cancer³³. Two cases accounting to approximately 1% of all the cases were reported from carcinoma cervix in our study.

12. Anal canal Cancer:

Lymphatic spread is the most common route of spread from anal cancer. Hematogenous spread of anal canal cancer develops in fewer than 10% of cases. Liver metastasis is more common than lung or bone metastasis and usually occurs in the case of a tumor arising at the anorectal junction⁵⁴. In the present study, two cases were reported with bone metastasis and the sites were lumbar spine and pelvis respectively.

13. Pancreas Cancer:

The usual sites of metastases in pancreatic cancer are the liver and peritoneal cavity. Other less common sites are the lung, bone, and brain⁵⁵. The first case of pancreatic cancer with skeletal metastases was stated in Russian literature⁵⁶ in 1963. Although the true incidence of skeletal metastases in patients with pancreatic cancer is not known, it is felt to be between 5 percent to 20 percent^{57,58}. In our study, we found only one case with bone metastasis which was multiple in origin involving dorsal and lumbar spine as well as long bone (femur).

14. Penile Cancer:

Penile cancer accounts to 1% of all male cancers and is usually localized cancer but metastasis do occurs in less than 3% patients⁵⁹. Bone metastasis, if present usually affects axial skeleton than appendicular skeleton and it is extremely rare⁶⁰. In our study, we found only one case with solitary metastasis to dorsal spine secondary to penile cancer.

15. Salivary Gland tumours:

Among salivary gland tumours, parotid gland tumour contributed to 2 cases with solitary metastasis to dorsal spine whereas submandibular carcinoma, although very rare⁶¹, one case was recorded with multiple metastases to lumbar spine and sacrum.

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