

Young Meds

Bone Cancer/Sarcoma

Cancer, we have a bone to pick with you.

Pooja Patil¹, Aditya Uchil¹, Jnana Krishnamsetty¹, Isabelle Zachariah¹

Cox Mill High School¹

Corresponding author: Dr. Lopamudra Das Roy Questions, please reach out: lopa@breastcancerhub.org

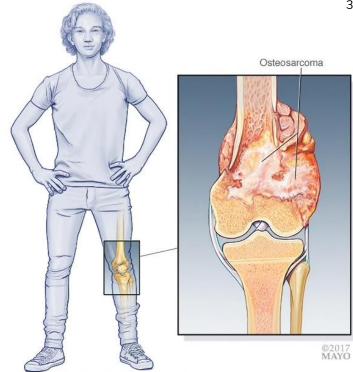
Abstract

Osteosarcoma makes up one quarter of all primary bone cancers diagnosed in the U.S. The researchers hope to allow for easy access to important information about Osteosarcoma. A variety of sources were used to gather data. The main databases used to find publications were PubMed, Cancer Net, American Cancer Society, and National Cancer Institute. Through these databases, it was proven that Osteosarcoma is more frequent within certain races and an estimated 3,500 people will be diagnosed with primary bone cancer in the U.S. this year. Osteosarcoma is a prevalent cancer which, with better knowledge, can be prevented or better diagnosed.



What is Osteosarcoma?

Osteosarcoma (also called osteogenic sarcoma) is the most common type of cancer that starts in the bones. The cancer cells are disguised as bone cells which makes up new bone tissue in bones but is significantly weaker than normal bone tissue $cells.^2$



COUNDATION FOR MEDICAL EDUCATION AND RESEARCH ALL DIGUTS RESERVE

Statistics

Less than 0.2% of all cancers are primary bone cancer. However, it is more common for bones to be the site of metastasis from other cancers. It is predicted that this year, 2019, an estimated 3,500 people of all ages in the US will be diagnosed with primary bone cancer and there will be 1,660 deaths. In adults, chondrosarcoma makes up more than 40% of primary bone cancers, followed by osteosarcoma (28%), chordoma (10%), Ewing sarcoma (8%), and UPS/fibrosarcoma (4%). The remaining types of bone cancer are rare. The cumulative 5-year survival rate for adults and children with bone cancer is 70%.⁴

Risk Factors and Causes

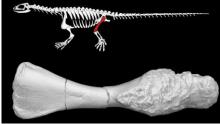
Although lifestyle-related risk factors play a major role in several adult cancers, this is not the case for osteosarcoma. The more prominent risk factors for osteosarcoma include age/height, gender, race/ethnicity, radiation, genetics, and previous bone diseases. Factors such as age and height suggest that rapid bone growth may link with the risk of tumor formation. In addition, osteosarcoma is more common in males than females, especially if they are Hispanic/Latino or African Americans. African Americans, as a result of their darker pigmentation, are more prone as well. People with previous exposure to radiation therapy for another cancer have an increased risk of developing bone cancer.⁵

Signs and Symptoms

Pain at the site increases as the tumor size increases and with weight bearing on the tumor site. As the tumor grows, the bone structure at the site is weakened. Patients often present with a pathologic fracture at diagnosis as a result of the tumor's effects. The pain has been characterized as an intermittent ache which then progresses to a persistent pain. When in the lower body, a limp is often present. When in the upper body, there is pain when lifting. The site will often present with tenderness, swelling, or redness. About two months after the initial pain, a soft tissue mass will often develop at the site. During the physical check for osteosarcoma, asymmetry of the affected extremity to the unaffected comparative extremity is a sign of osteosarcoma being present.⁶

History

Human beings and animals have had cancer throughout history and evidence can be found among fossilized bone tumors, human mummies, and ancient manuscripts. The Edwin Smith Papyrus was discovered in 3000 BCE and is a copy of part of an ancient Egyptian textbook on trauma surgery. The writing says about the disease, "There is no treatment." Over time, the treatment for bone cancer became more advanced with developments such as chemotherapy and radiation therapy.⁷



Types of Bone Cancers

Malignant (cancerous) bone tumors⁸

- Chondrosarcoma (cancer that develops from cartilage)
- Malignant fibrous histiocytoma (MFH) of bone, also known as undifferentiated pleomorphic sarcoma of bone
- Fibrosarcoma
- Chordoma
- Malignant giant cell tumor of bone

Benign (non-cancerous) bone tumors⁸

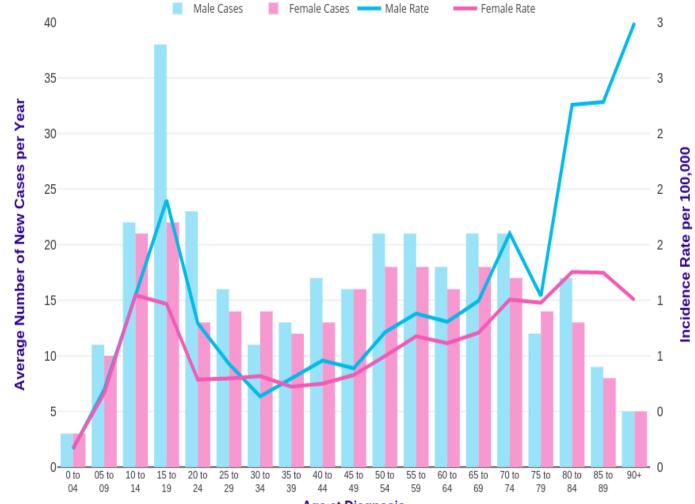
- Osteoma
- Chondroma
- Osteochondroma
- Lymphangioma
- Benign Tumors can be malignant. They don't spread but can reappear in different areas.

Stages

³The tumor begins at the origin, which is primarily in the cells that form bones. It also can occur in soft tissues surrounding the bone, known as periosteum. As bone cancer can start in any bone throughout the body, it most commonly affects the pelvis or long bones such as the arms and legs. As a type of bone cancer, Osteosarcoma tends to develop in young adults or teenagers, but it can also occur in children and adults. ⁹Osteosarcoma is present in 2.4% of childhood cancers. It is determined by a malignant osteoid and is primarily in the metaphysis of long tubular bones of young patients, from 15 to 19 years of age. ¹⁰Once developed, the tumor becomes metastatic and spreads from the origin to the lungs or more bones. Once diagnosed, patients will receive treatment which has shown to be difficult with cumulative amounts of surgery, chemotherapy, radiotherapy, etc...

Ethnicity and race

The link between ethnicity and causes of bone cancer, such as Osteosarcoma, has not been looked into with great detail. However, specific studies with patients less than 19 years of age were analyzed and they displayed that Hispanic patients seemed to be significantly more likely to contract metastatic disease at presentation of Osteosarcoma - rather than non Hispanic patents (Hispanic-27.2% vs. non-Hispanic 20.3%). The conclusion of the study showed that Hispanic patients are more likely to have advanced diseases in Osteosarcoma. Osteosarcoma is more prevalent in African Americans as well as Hispanic/Latino people rather than Caucasians. For Hispanics 0-14 years of age there has shown to be a 4.2% incidence rate for Osteosarcoma; whereas, Non-Hispanics showed to have a 3.7% incidence rate. For patients 15-19 years of age, Hispanic patients displayed 8.2% prevalence as compared to 7.6% for Non-Hispanic cases.⁴



Age at Diagnosis

11

Genetics

¹²The "Li-Fraumeni" syndrome is caused by inherited mutations which turn off the TP53 tumor suppressor gene. ⁵Patients that were diagnosed with Osteosarcoma (less than 30 years of age) 3.8% carried an LFS-associated mutation in the TP53 gene, while 5.7 percent carried a very rare TP53 variation of the specific gene. There was a cumulative presence of TP53 mutations which came to 9.5%, noticeably larger than past studies. It has been found that nearly 4 percent of cases involving pediatric Osteosarcoma "have a LFS-associated germline TP53 mutation," and this has become an important factor since it may cause risk for the patients family members for developing other types of LFS-associated cancers. ¹³While these are all potential risks to the diagnosis of bone cancer and Osteosarcoma genetic aberrations in gene expression in the tissue have not yet identified a common of recurrent genetic alteration that explains the progression of the tumor.

Metastasis

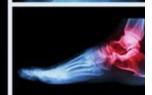
Metastasis is the stage at which the tumor spreads to other parts of the body. Metastatic osteosarcoma may have tumors present in various organs throughout the body, but most often in the lungs. One-fifth of the osteosarcomas detected are often already metastatic in nature by the time of diagnosis. This makes it harder to treat, but can still be cured if surgically operable. The rate of success for such surgeries improves noticeably if in conjunction with chemotherapy.¹⁴

Current Treatment Modules (Before)

The types of treatment options for bone cancer include: surgery, chemotherapy and radiation therapy. Most often, chemotherapy is given both before and after surgery. It can assist in lowering the risk that cancer will come back after treatment. It may also allow for a less extensive operation to remove cancer. Surgery is an important part of treating bone cancer as it includes two stages: the biopsy to diagnose the cancer and the surgical treatment to remove the cancer. The main goal of surgery is to remove all cancer causing cells because even if a few remain, they can grow and multiply to form a new tumor. Radiation therapy is for the cases where the tumor can't be removed completely by surgery such as in the bones of the face.¹⁵





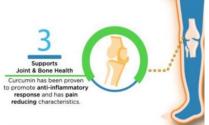


After treatment, it is important for the patient to attend all follow-up appointments. Visiting the oncologist and the orthopedic surgeon to get scans every few months during the first couple of years after treatment, and less often after is important to make sure there are no issues. Physical therapy and rehabilitation are also a very crucial part of recovery after treatment. Some chemotherapy drugs can cause problems with hearing or heart damage. People who get these drugs may also have tests to review hearing or heart function.¹⁷

(Relations between) arthritis (or inflammation) and bone cancer

The symptoms of bone cancer and arthritis are similar. Both have the symptom of pain in the bone. The pain from bone cancer is not constant, it is worse at night and when the bone is used. As the cancer grows, the pain grows as well. Swelling from the cancer does not occur immediately and the mass may not be observable until weeks after the cancer forms. Bone cancer also weakens the bone that it is in, similar to arthritis.¹⁴

Any adjuvants used in addition to the primary treatments involving radiation, chemotherapy, (curcumin?)



- Curcumin is an adjuvant. It possesses anti-inflammatory and antioxidants that can be used to prevent particular diseases such as arthritis, bone cancers, hyperlipidemia, including breast cancer.¹⁸
- High-dose methotrexate, Adriamycin, and cisplatin can treat cancer.¹⁹
- Neoadjuvant chemotherapy refers to medicines that are administered before surgery. Doctors may recommend neoadjuvant chemotherapy due to the size of the tumor, since the drugs may shrink the tumor and give you more surgical options.¹⁹

Resources

¹ payment, One-time, et al. "Sarcoma and Bone Cancer Ribbon Vector Image on VectorStock." VectorStock,

https://www.vectorstock.com/royalty-free-vector/sarcoma-and-bone-cancer-ribbon-vector-7519527.

²"What Is Osteosarcoma?" American Cancer Society, <u>www.cancer.org/cancer/osteosarcoma/about/what-is-osteosarcoma.html</u>.

³"Osteosarcoma." Mayo Clinic, Mayo Foundation for Medical Education and Research, 30 Jan. 2018, <u>https://www.mayoclinic.org/diseases-conditions/osteosarcoma/symptoms-causes/syc-20351052</u>.

⁴"Bone Cancer - Statistics." Cancer.Net, 8 Apr. 2019, <u>www.cancer.net/cancer-types/bone-cancer/statistics</u>.

- ⁵"What Causes Osteosarcoma?" American Cancer Society, <u>www.cancer.org/cancer/osteosarcoma/causes-risks-prevention/what-causes.html</u>.
- ⁶Hiller, Chelsea, et al. "Osteosarcoma: Accurately Diagnosing This Bone-Chilling Disease." JAAPA : Official Journal of the American Academy of Physician Assistants, U.S. National Library of Medicine, Dec. 2016, <u>www.ncbi.nlm.nih.gov/pubmed/27846188</u>.
- ⁷"Early History of Cancer." American Cancer Society, www.cancer.org/cancer/cancer-basics/history-of-cancer/what-is-cancer.html. ⁸"What Is Osteosarcoma?" American Cancer Society, www.cancer.org/cancer/osteosarcoma/about/what-is-osteosarcoma.html.
- ⁹"Article Tools." Journal of Clinical Oncology, ascopubs.org/doi/abs/10.1200/jco.2014.32.15_suppl.1614.
- ¹⁰"Osteosarcoma Childhood and Adolescence Stages." Cancer.Net, 17 May 2019, <u>www.cancer.net/cancer-types/osteosarcoma-childhood-and-adolescence/stages</u>.
- ¹¹"Bone Sarcoma Incidence Statistics." Cancer Research UK, 18 July 2019, <u>https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/bone-sarcoma/incidence</u>.
- ¹²"Osteosarcoma TP53 Inherited Gene Mutation Adolescents." National Cancer Institute, <u>www.cancer.gov/news-events/press-</u> releases/2015/osteosarcoma-tp53-inherited-gene-mutation-adolescents.
- ¹³Morrow, James J, and Chand Khanna. "Osteosarcoma Genetics and Epigenetics: Emerging Biology and Candidate Therapies." Critical Reviews in Oncogenesis, U.S. National Library of Medicine, 2015, <u>www.ncbi.nlm.nih.gov/pmc/articles/PMC4894524/</u>.
- ¹⁴"Signs and Symptoms of Bone Cancer." American Cancer Society, <u>www.cancer.org/cancer/bone-cancer/detection-diagnosis-</u> <u>staging/signs-symptoms.html</u>.
- ¹⁵"Treating Osteosarcoma." American Cancer Society, <u>www.cancer.org/cancer/osteosarcoma/treating.html</u>.
- ¹⁶(http://digitaladvisor.nz/), Digital Advisor. "Bone Cancer." Bone Cancer | Auckland Radiation Oncology, https://aucklandradiationoncology.co.nz/understanding/bone-cancer/.
- ¹⁷"Living as an Osteosarcoma Survivor." American Cancer Society, <u>www.cancer.org/cancer/osteosarcoma/after-treatment/follow-up.html</u>.
- ¹⁸"Curcumin Is an APE1 Redax Inhibitor and Exhibits an Antiviral Activity against KSHV Replication and Pathogenesis." Antiviral Research, Elsevier, 26 Apr. 2019, <u>www.sciencedirect.com/science/article/pii/S0166354218307253?via%3Dihub</u>.
- ¹⁹Labs, Wonder. "6 Benefits of Adding Turmeric Extract w/ Curcumin to Your Diet." WonderLabs, <u>https://www.wonderlabs.com/blog/6-benefits-of-adding-turmeric-extract-w-curcumin-to-your-diet</u>.
- ²⁰Li, He, et al. "Curcumin Is an APE1 Redox Inhibitor and Exhibits an Antiviral Activity against KSHV Replication and Pathogenesis." Antiviral