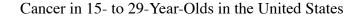
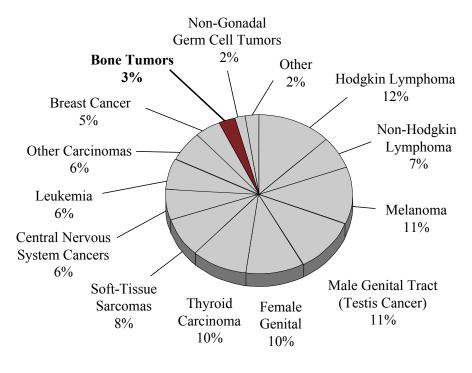
Chapter 8

Malignant Bone Tumors





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HIGHLIGHTS

Incidence

- Primary neoplasms of the bone are uncommon in adolescents and young adults and accounted for 3% of all neoplasms in this age group. Osteosarcoma was the most frequent malignant bone tumor (approximately 47% of all bone neoplasms among 15- to 29-year-olds) followed by Ewing sarcoma/peripheral primitive neuroectodermal tumor (pPNET *of bone*) (27%) and chondrosarcoma (15%).
- In 15- to 29-year-olds, as in children and young adolescents, most osteosarcomas occurred in the metaphyses of long bones and particularly the distal femur, proximal humerus and proximal tibia. In Ewing sarcoma and chondrosarcoma, however, the central axis was the most frequent site of disease; these diseases had a remarkably similar anatomical distribution.
- The average annual incidence of bone cancer peaked at 15 per million in those 15 to 19 years of age, and fell to 6 per million by 25 to 29 years of age.
- Bone cancer in males occurred at a rate almost double that of females in the 15- to 19-year age group—approximately 200 per year. There were approximately 100 patients a year diagnosed with Ewing sarcoma/pPNET from 15 to 19 years of age, two-thirds of whom were males. Osteosarcomas occurred at an earlier age in females than in males.
- The incidence of osteosarcoma in males was higher than in females for all ages except those younger than 9 years. Ewing sarcoma/pPNET was also more common in males, with a lower predominance than osteosarcoma.
- Between 1975 and 1999, the incidence of osteosarcoma increased at an average of 1.4% per year (p <0.05) in the 15to 29-year age group. In contrast, the incidence of Ewing sarcoma remained stable during the past quarter century.
- Ewing sarcoma/pPNET occurred predominantly in white non-Hispanics and Hispanics, with a lower incidence in Asians/Pacific Islanders. Over the age of 30, Ewing sarcoma/pPNET occurred almost exclusively in white non-Hispanics. Osseous Ewing sarcoma rarely occurred in the African American/black population.

Mortality & Survival

- Mortality for bone tumors in adolescents and young adults was higher in males than females over the adolescent and young adult age range and much higher than expected in 20- to 24-year-olds, even taking into consideration the higher incidence in males than females.
- The U.S. bone cancer mortality was highest for males and females 15 to 19 years of age.
- The survival rate for all bone sarcomas was similar across age groups, with an overall modest improvement in survival from 1975 to 1980 and from 1993 to 1998.
- In the U.S., the 5-year survival rates for osteosarcoma and Ewing sarcoma were comparable among 15- to 29-yearolds, about 60% for the most recent era. Survival rates for chondrosarcoma exceeded 90% in the most recent era.
- Patients with osteosarcoma between the ages of 30 and 44 years had a slightly better outcome than patients aged 15 to 29 years, the reasons for which are unclear. Patients with osteosarcoma who were older than 45 years of age had a poorer outcome than all other age groups.
- Patients with Ewing sarcoma, regardless of age, showed an overall improvement in survival from 1975 to 1998.

Risk Factors

- Known risk factors for osteosarcoma are ionizing radiation, alkylating agents, Paget disease, hereditary retinoblastoma, Rothmund –Thomson syndrome, Werner syndrome, Bloom syndrome and the Li-Fraumeni familial cancer syndrome.
- Ionizing radiation has been implicated as a causative factor in approximately 3% of osteosarcomas.
- Aside from the difference in incidence by race/ethnicity (whites have a much higher incidence than African Americans/blacks), there are no known risk factors for Ewing sarcoma/pPNET.
- For chondrosarcoma, Marfucci's syndrome, Ollier's disease, multiple osteochondromatosis and hereditary multiple exostoses are the few known risk factors.

INTRODUCTION

Malignant bone cancers are sarcomas of bone, cartilage and associated tissues such as endothelial and neuroectodermal cells that participate in bone formation and maintenance. The Ewing family of tumors is particularly fascinating since the cell of origin remains uncertain and both soft-tissue and osseous forms are known to exist. Although they are among the relatively infrequent cancers in individuals 15 to 29 years of age, they have special significance in this age group. In these older adolescents and young adults, two tumors alone-osteosarcoma and Ewing sarcoma-account for three-fourths of all bone cancer. And if the next most common bone cancer in this age group-chondrosarcoma-is included, the three account for more than 90% of all bone cancer diagnosed. The older adolescent and young adult years are those during which the incidence of Ewing sarcoma declines dramatically and that of chondrosarcoma increases, such that by age 25 to 30 these two types of bone cancer are approximately equal in incidence. The treatment of bone cancer is highly challenging to the young adult or adolescent patient, since amputation and extensive surgical procedures such as limb salvage and hemipelvectomies are often necessary.

METHODS, CLASSIFICATION SYSTEM, AND BIOLOGICAL IMPLICATIONS

In the International Classification of Childhood Cancer (ICCC), malignant bone tumors are described in category VIII. There are 5 subdivisions in VIII: *osteosarcoma* (VIII(a)), *chondrosarcoma* (VIII(b)), *Ewing sarcoma* (VIII(c)), *other specified malignant bone tumors* (VIII(e)), and *unspecified malignant bone tumors*. The emphasis in this chapter is on subgroups (a), (b), and (c).

Osteosarcomas derive from primitive bone-forming mesenchymal stem cells and most often occur in the metaphyseal portions of long bones,^{1,2} especially during the first decades of life. *Osteosarcoma*, the most common bone cancer in adults, is category VIII(a) in the ICCC based on ICD-O codes 9180-9200 at any site in the body. This includes osteosarcoma [NOS (9180), chondroblastic (9181), fibroblastic (9182), telangiectatic (9183), in Paget disease (9184), small cell (9185), juxtacortical (9190)] and osteoblastoma (9200). New histologies that also fall into VIII(a) from

ICD-O-3 are: central osteosarcoma (9186), intraosseous well differentiated osteosarcoma (9187), periosteal osteosarcoma (9193), high grade surface osteosarcoma (9194), and intracortical osteosarcoma (9195).

Chrondrosarcoma, the second most common of the bone malignancies in older adults,³ is category VIII(b) in the ICCC. The equivalent ICD-O categories are chondrosarcoma [NOS (9220), juxtacortical (9221)] and malignant chondroblastoma (9230) for all sites in the body, and myxoid chondrosarcoma (9231) and mesenchymal chondrosarcoma (9240) for bones, joints and articular cartilage of limbs. New histologies that also fall into VIII(b) from ICD-O-3 are clear cell chondrosarcoma (9242) and dedifferentiated chondrosarcoma (9243).

The *Ewing Sarcoma Family of Tumors* includes Ewing, atypical Ewing, and peripheral primitive neuroectodermal tumor (pPNET) of bone. These tumors are believed to be of neural crest origin and to also occur in soft tissue sites. The latter occurrences are not included in this chapter (cf. Soft Tissue Sarcomas), albeit they may occur at virtually any site in the body. As osseous tumors, Ewing sarcoma occurs at approximately equal incidence in the extremities and central axis.⁴ Ewing sarcoma is category VIII(c) in the ICCC: 9260 (classic Ewing tumor), 9363 (malignant melanotic neuroectodermal tumor), and the SEER modification adds 9473 (primitive neuroectodermal tumor (PNET) of bone and joints.

Other Specified Malignant Bone Tumors are category VIII(d) in the ICCC and ICD-O categories 8812 (periosteal fibrosarcoma), 9250 (malignant giant cell tumor of bone), 9261 (adamantinoma of long bones), 9270-9330 (malignant odontogenic tumors), and 9370 (chordoma, NOS). Malignant tenosynovial giant cell tumor (ICD-O-3 9252) is included with fibrous histiocytoma (8830) in ICCC IX(b). Unspecified Malignant Bone Tumors are category VIII(e) in the ICCC, which includes histologies commonly indicative of soft tissue sarcoma that have arisen in bone (8800-8804) and unspecified malignant tumors (8000-8004).

As explained in the *Methods* chapter, data are presented for 15- to 29-year-olds with comparisons to the age

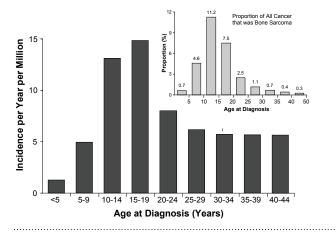


Figure 8.1: Incidence of All Bone Sarcomas, SEER 1975-1999

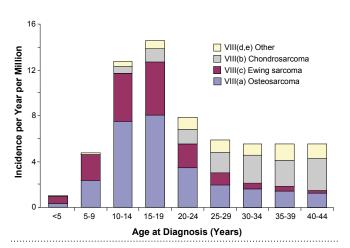


Figure 8.2: Incidence of Bone Sarcomas by Type, SEER 1975-2000

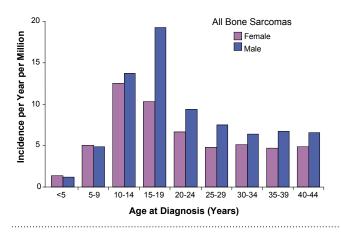


Figure 8.3: Incidence of All Bone Sarcomas by Gender, SEER 1975-1999

groups 0 to 15 years and 30 to 44+ years, as appropriate. For some analyses the entire age range from birth to 85+ years is included. The absence of data in any figure or table within this chapter means that too few cases were available for analysis; it does not mean that the rate or change in rate was zero.

INCIDENCE

As estimated from SEER data and the U.S. 2000 census, the average incidence of bone cancer in adolescents and young adults 15 to 29 years of age was 9.8 per year per million persons. The histology-specific rates were 4.6 per million for osteosarcoma, 2.6 per million for Ewing sarcoma and 1.5 per million for chondrosarcoma.

Bone tumors are classified as osteosarcoma, Ewing sarcoma, chondrosarcoma, "other specified malignant bone tumor" and "unspecified malignant bone tumor."¹ The three most common bone cancers in 15- to 29-year-olds are osteosarcoma, Ewing sarcoma, and chondrosarcoma, which account for 48%, 27% and 15% of bone cancers in the age group, respectively. From the trends in incidence for the 25-year period from 1975 to 2000, an estimated 325, 163 and 109 15- to 29-year-olds were diagnosed in the U.S. with osteosarcoma, Ewing sarcoma, and chondrosarcoma, respectively (Table 8.1).

Age-Specific Incidence

Bone cancer represented only 3% of all malignancies in the 15- to 29-year age group. It accounted for 7.5% of all cancers in those 15 to 19 years, 2.5% for those 20 to 24 years, and 1.1% for 25- to 29-year olds (Figure 8.1; inset). The incidence of bone cancer peaked at 15 per year per million for those 15 to 19 years of age, and then fell to 8 per year per million for 20- to 24-year-olds and 6 per year per million for those 25 to 29 years of age (Figure 8.1). Figure 8.2 displays specific rates for specific histologic subtypes according to the different age groups.

Gender-Specific Incidence

The incidence of malignant bone tumors was higher in males than in females in the adolescent and young adult population (Figure 8.3); both osteosarcoma and Ewing sarcoma had a higher incidence in males (Figures 8.4 and 8.5). The remaining types of malignant bone tumors, in aggregate, also demonstrated a male predominance (Figure 8.6).

Racial/Ethnic Differences in Incidence

Figure 8.7 depicts the comparable incidence of bone cancer among various racial/ethnic groups over the past decade. The overall incidence for white non-Hispanics in the 15- to 29-year age group was slightly higher, 11.3 per year per million, in comparison to incidence for other races/ethnicities-8.1, 10.2, and 9.1 per year per million for African Americans/blacks, Hispanics, and Asians/ Pacific Islanders, respectively (Figure 8.7). However, this was not true across histological subtypes. For osteosarcoma, Hispanics had the highest incidence in those 15 to 29 years of age (Figure 8.8). For Ewing sarcoma, racial variation was dramatic. There was no discernable incidence of Ewing sarcoma in African Americans/ blacks and Asians/Pacific Islanders over 15 years of age. For those over 30 years of age, this disease occurred nearly exclusively in the white non-Hispanic population

(Figure 8.9). An absence of Ewing sarcoma has also been observed in several African countries.⁵ The underlying biological mechanism behind these observations is yet to be elucidated (see *Risk Factors* section).

Trends in Incidence

The incidence of osteosarcoma, Ewing sarcoma and all bone cancers, according to 5-year periods between 1975 and 1995, is shown in Table 8.2.

Figure 8.10 (left panel) shows an increase in the incidence of malignant bone tumors of 0.92% per year (p < 0.05) during the period 1975 to 1999 in the adolescent and young adult population as compared to children < 15 years of age. This increase was due to more male patients being diagnosed, the reasons for which are unclear. Histologyspecific incidence by single year of diagnosis for 1975 to

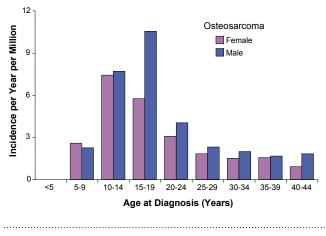
Table 8.1: Incidence of Malignant Bone Tumors in Persons Younger Than 30 Years of Age, U.S., 1975-2000

AGE AT DIAGNOSIS (YEARS)	<5	5-9	10-14	15-19	20-24	25-29
U.S. population, year 2000 census (in millions)	19.176	20.550	20.528	20.220	18.964	19.381
ALL MALIGNANT BONE TUMORS						
Average incidence per million, 1975-2000, SEER	1.3	5.0	13.1	14.8	8.0	6.2
Average annual % change in incidence, 1975-2000, SEER	٨	1.4%	0.9%	1.0%	1.0%	2.2%
Estimated incidence per million, year 2000, U.S.	٨	5.7	14.5	16.5	9.0	7.5
Estimated number of persons diagnosed, year 2000, U.S.	٨	118	298	333	170	146
OSTEOSARCOMA						
Average incidence per million, 1975-2000, SEER	0.4	2.4	7.6	8.2	3.5	2.1
Average annual % change in incidence, 1975-2000, SEER	٨	1.0%	1.8%	1.1%	1.5%	4.8%
Estimated incidence per million, year 2000, U.S.	٨	10.8	9.0	9.4	4.2	2.8
Estimated number of persons diagnosed, year 2000, U.S.	٨	65	184	190	80	55
EWING SARCOMA						
Average incidence per million, 1975-2000, SEER	0.6	2.3	4.3	4.6	2.1	1.9
Estimated incidence per million, year 2000, U.S.	٨	2.0	4.1	5.1	2.1	1.1
Estimated number of persons diagnosed, year 2000, U.S.	٨	41	85	103	39	21
CHONDROSARCOMA						
Average incidence per million, 1975-2000, SEER	٨	0.1	0.6	1.2	1.3	1.9
Average annual % change in incidence, 1975-2000, SEER	٨	3.3%	2.8%	-20.5%	4.9%	3.3%
Estimated incidence per million, year 2000, U.S.	٨	0.2	0.7	1.3	1.7	2.5
Estimated number of persons diagnosed, year 2000, U.S.	٨	3	15	27	33	49

^Too few for a reliable estimate

	1975-80	1981-86	1987-92	1993-99
OSTEOSARCOMA	4.1	4.6	5.1	5.2
EWING SARCOMA	2.4	3.1	2.7	2.8
CHONDROSARCOMA	1.4	1.2	1.5	1.6
ALL BONE CANCER	8.7	9.9	10.2	10.7

Table 8.2: Average Age-Adjusted Incidence per Year per Million for All Malignant Bone Tumors, All Races/Ethnicities, BothGenders, Age 15 to 29 Years, SEER 1975-1995



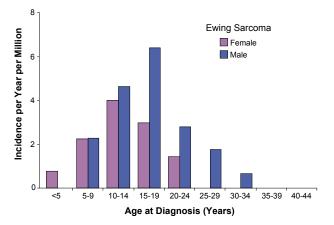


Figure 8.4: Incidence of Osteosarcoma by Gender, SEER 1975-1999

1999 revealed that this increase was predominantly due to an increase in the rate of osteosarcomas in 15- to 29year-olds, an increase averaging 1.4% per year (p < 0.05) (Figure 8.11, right panel). The increase in osteosarcoma incidence was inversely proportional to age in those 15 to 29 years of age, with an average percent increase of 2.3%, 2.2%, and 0.7% per year from 1975 to 1999 for 15- to 19-year-olds, 20- to 24-year-olds, and 25- to 29-year-olds, respectively (Table 8.1). There was no discernable change in the osseous Ewing sarcoma incidence during the same interval, despite the development of the concept of a Ewing family of tumors, including PNET of soft tissue.

Bone Cancer Location

The most frequent site of bone cancer development was the long bone of the lower limb. The site distribution of Ewing sarcomas, however, differed substantially from that of osteosarcomas and chondrosarcoma (Figure 8.11). In 15to 29-year-olds, as in children and young adolescents, most osteosarcomas occurred in the metaphyses of long bones and particularly the distal femur, proximal humerus and proximal tibia. In Ewing sarcoma and chondrosarcoma,

Figure 8.5: Incidence of Ewing Sarcoma by Gender, SEER 1975-1999

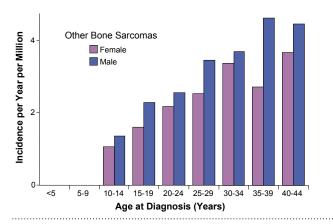


Figure 8.6: Incidence of Other Bone Sarcomas by Gender, SEER 1975-1999

however, the central axis (vertebral column, ribs, sternum, clavicle, pelvis, sacrum and coccyx) was the most frequent site. Ewing sarcoma and chondrosarcoma had a remarkably similar anatomical distribution, with the only major difference being that chondrosarcoma had an increased occurrence in the calvarium and decreased incidence in the spine (Figure 8.11).

OUTCOME

Mortality

Mortality for all bone tumors was highest-approximately 8 deaths per million—for patients 15 to 24 years of age, especially for males, and lowest-less than 1 death per million-for patients younger than 9 years of age (Figure 8.12). In all age categories over 15 years, mortality for males was greater than that for females. In general, these differences reflect incidence patterns. They are, however, out of proportion to the trends in incidence; the mortality rate is higher than expected among 15- to 29year-olds. This is indicated by the ratio of mortality rate to incidence as a function of age (Figure 8.13). The excess mortality rate was particularly apparent in males who were 20 to 24 years of age. This is borne out by the average rate of reduction in mortality, which was less significant for patients 15 to 44 years of age than in younger or older persons (Figure 8.14).

When evaluated according to race/ethnicity, mortality from malignant bone tumors during the period 1990 to 2000 was not significantly different among the different racial/ethnical groups (Figure 8.15), and where comparable, was generally reflective of incidence patterns.

Survival

Long term survival varied remarkably among the three major types of bone tumors that occur in 15- to 29-year-olds (Figure 8.16). Chondrosarcoma had the best survival, exceeding 75% at 20 years. Ewing sarcoma (and other peripheral primitive neuroectodermal tumors) had the

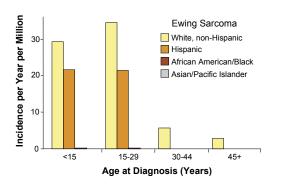
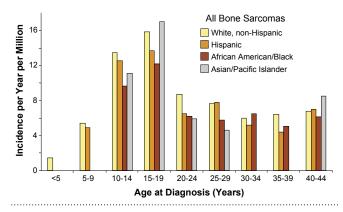
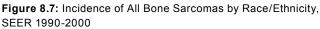
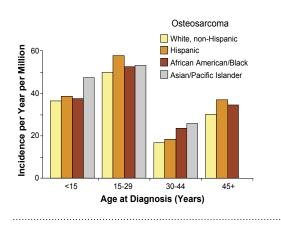
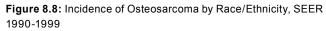


Figure 8.9: Incidence of Ewing Sarcoma by Race/Ethnicity, SEER 1990-1999









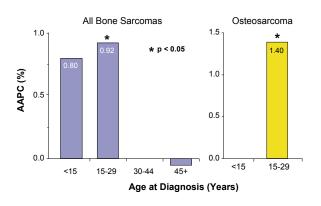


Figure 8.10: Average Annual Percent Change (AAPC) in Incidence of All Bone Sarcomas and Osteosarcoma, SEER 1975-1999

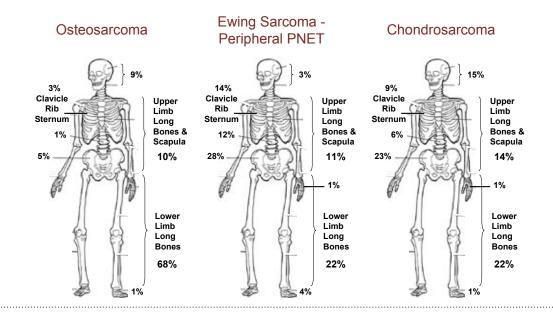


Figure 8.11: Most Frequent Sites of Bone Cancer Development in 15- to 29-Year-Olds, SEER 1992-2002. Drawings by Mascape

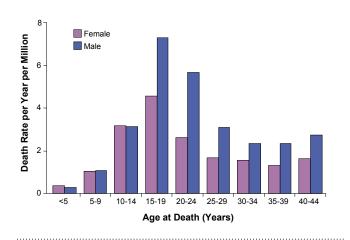


Figure 8.12: National Mortality by Gender for All Bone Sarcomas, U.S., 1975-1999

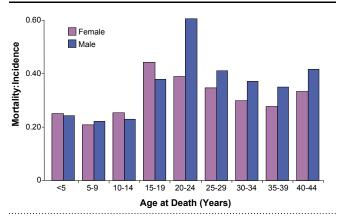


Figure 8.13: Ratio of National Mortality to SEER Incidence for All Bone Sarcomas by Gender, U.S., 1975-1999

worst survival, approximately 30% at 20 years. Osteosarcoma had a lower survival rate after 4 years of followup. Chondrosarcoma and osteosarcoma showed a plateau on their survival curves, suggesting that cure of the disease was achieved in nearly all patients by ten years. The Ewing sarcoma survival curve did not reveal a plateau, indicating that very late relapses of this malignancy were not uncommon.

For osteosarcoma, the survival curves for the age groups younger than 45 were nearly identical from 1975 to 2000 (Figure 8.17). In older patients, survival was considerably worse, approximately half that of patients younger than 45. For those diagnosed with Ewing sarcoma between 15 and 30 years of age, long-term survival was about half that of children and young adolescents diagnosed during the same era, and not unlike long-term survival for older patients (Figure 8.18). Patients with chondrosarcoma had a better survival than those with either osteosarcoma or Ewing sarcoma, regardless of age (Figure 8.19). Survival rates for 15- to 29-year-olds with chondrosarcoma were not as high as for 30- to 44-year-olds, although at 18 years from diagnosis both survival curves converged.

Survival for patients younger than 45 years with bone tumors has seen a modest but constant improvement, from less than 60% in the 1975 to 1980 treatment era, to greater

than 70% in the 1993 to 1998 treatment era (Figure 8.20). The 30- to 44-year age group had the highest survival rate in all treatment eras, with survival reaching almost 80% since 1987. This improvement in survival over time has also been noted for patients with osteosarcoma (Figure 8.21) and Ewing sarcoma (Figure 8.22), although survival rates for 15- to 29-year-olds were lower than for younger children in the latter group. The 5-year survival rates for patients younger than 45 years of age with osteosarcoma was greater than 65%, but continued to be less than 45% for the 45 year and older age group. The 5-year survival rate for patients younger than 15 years of age with Ewing sarcoma has improved to greater than 65%. However, the 5-year survival rate remains less than 50% for those older than 15 years of age. Patients with chondrosarcoma did not show a consistent trend in survival improvement, albeit evidence for some progress is apparent in those who were over 45 years of age at diagnosis (Figure 8.23).

Small differences in 5-year survival rates for all bone tumors were noted for the different racial/ethnic groups (Figure 8.24). For those younger than 15 years of age, the highest survival rate was observed in white non-Hispanics, at almost 80%. The lowest survival rate was observed in Hispanics at approximately 60%. In the 15- to 29-year age group, no significant survival differences were seen. In the 30- to 44-year age group, the survival was almost 80% for white non-Hispanics and Asians/Pacific Islanders, and nearly 60% for African Americans/blacks. The lowest survival rates were for the 45-year and older age groups. The 5-year survival rate for white non-Hispanics was 60%, decreasing slightly for Hispanics, African Americans/blacks and Asians/Pacific Islanders.

RISK FACTORS

There are few known risk factors for bone sarcomas. Certain genetic susceptibility syndromes (hereditary retinoblastoma, Li-Fraumeni syndrome, Rothmund-Thomson syndrome, and Werner syndrome) and prior treatment for childhood cancer with radiation and/or chemotherapy have all been shown to increase the risk of osteosarcoma,⁶⁻¹⁴ but these factors account for a small proportion of cases. The descriptive epidemiology of osteosarcoma also strongly suggests an etiology related to pubertal development and bone

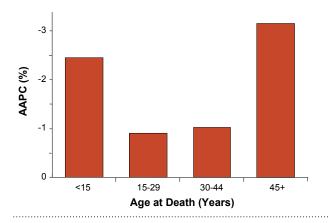
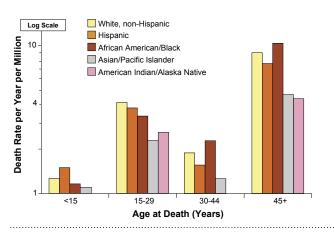
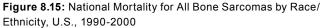
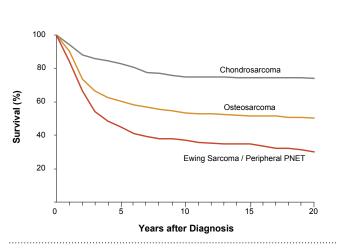
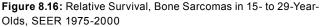


Figure 8.14: Bone Sarcomas, Average Annual Percent Change (AAPC) in National Mortality, U.S., 1975-1999









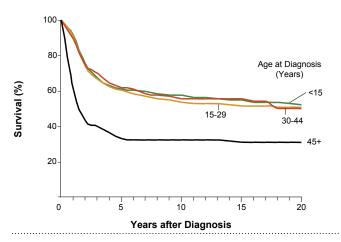


Figure 8.17: Relative Survival by Age, Osteosarcoma, SEER 1975-2000

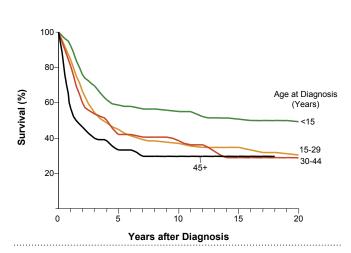


Figure 8.18: Relative Survival by Age, Ewing Sarcoma & Peripheral Primitive Neuroectodermal Tumors, SEER 1975-2000

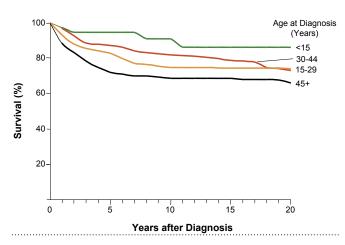


Figure 8.19: Relative Survival by Age, Chondrosarcoma, SEER 1975-2000

growth.¹⁵ However, analytic studies of height, the rate of bone growth, and the timing of puberty have been inconsistent.¹⁶⁻²¹ The only known risk factor for Ewing sarcoma is race/ethnicity (see Figure 8.9). The rate of Ewing sarcoma in whites is nearly nine times that of African Americans/blacks.^{18,22,23} While these data are consistent with a genetic predisposition, no associations of Ewing sarcoma with congenital syndromes are apparent. Intriguingly, four studies have found an association between Ewing sarcoma and hernia,²⁴⁻²⁷ while a fifth did not.¹⁸ The consistency of the association, given the small size of the literature and the memorable nature of the exposure, make these findings credible. Genetic syndromes such as Marfucci's syndrome, Ollier's disease, multiple osteochondromatosis, and hereditary multiple exostoses are the few known risk factors for chondrosarcoma.²⁸⁻³⁰

SUMMARY

In this descriptive analysis of the population-based SEER data, bone cancer represented about 3% of malignancies in the adolescent and young adult population, with an average annual incidence of 9.8% over the time period 1975 to 1999. Incidence declined with increasing age from 15 to 44 years. Rates differed by gender in the adolescent and young adult group, with incidence in males higher than in females. Osteosarcoma and Ewing sarcoma were the most common malignancies

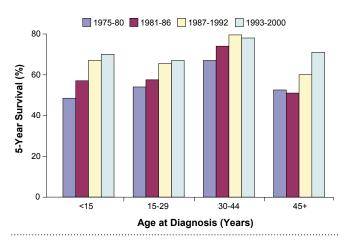
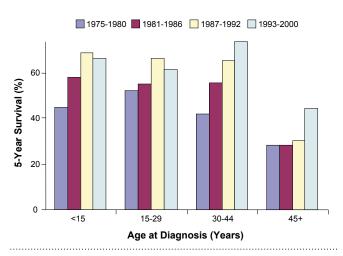
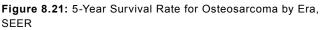


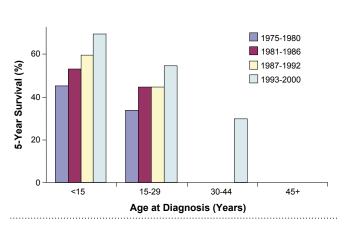
Figure 8.20: 5-Year Survival Rate for All Bone Sarcomas by Era, SEER

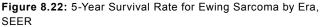
CHAPTER 8

of bone in adolescents and young adults. There were no significant racial/ethnic differences in the incidence of osteosarcoma. However, Ewing sarcoma was dramatically higher in the white population. The most common site for the development of osteosarcoma was the long bones of the lower limbs, while Ewing sarcomas and chondrosarcomas were more common in the central axis. The incidence of bone cancer has increased minimally, mainly due to an increase in the number of male patients with osteosarcoma. The etiology of bone cancer remains uncertain and few risk factors have been identified, which explain only a very small proportion of these cancers. The 5-year relative survival for adolescents and young adults with bone cancer improved from 54% in the time period 1975 to 1980 to 67% in the period 1993 to 1998. In general the 5-year survival for osteosarcoma is slightly better than for Ewing sarcoma. Males and females appear to have equal survival for both diseases.









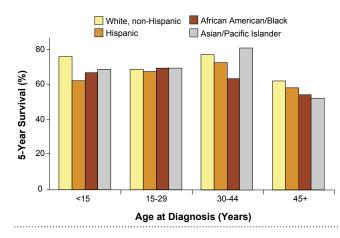


Figure 8.24: 5-Year Survival Rate for All Bone Sarcomas by Race/Ethnicity, SEER 1975-1999

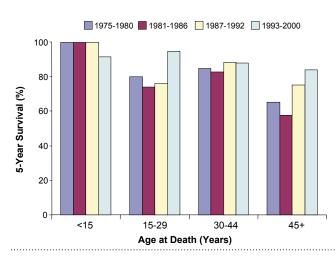


Figure 8.23: 5-Year Survival Rate for Chondrosarcoma by Era, SEER

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