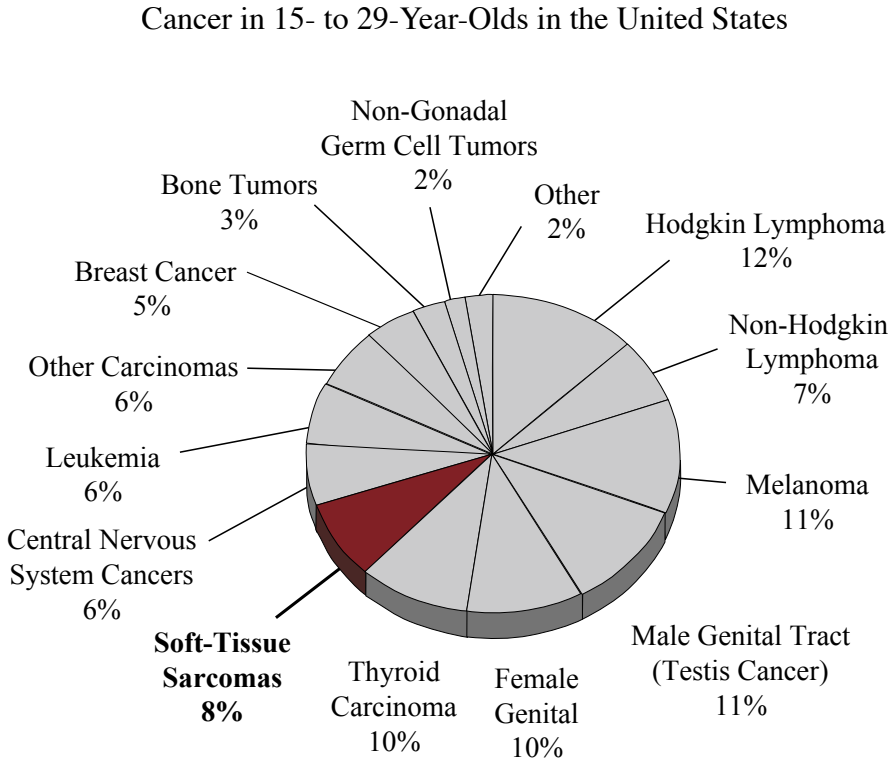
Chapter 7

Soft Tissue Sarcomas



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HIGHLIGHTS

Incidence

- Soft tissue sarcomas may occur at any age, but predominate in young adulthood. Over the period 1975 to 1999, the incidence of non-Kaposi soft tissue sarcoma increased exponentially in those older than 15 years of age.
- In the year 2000, approximately 1,700 Americans 15 to 29 years of age developed a non-Kaposi soft tissue sarcoma.
- In the 15- to 29-year age group there were far more histologic types of soft tissue sarcoma than in younger patients, with fibrosarcomas and related fibromatous entities constituting the largest histologic group.
- African Americans/blacks between the ages of 5 and 45 had a higher incidence of both non-Kaposi and Kaposi soft tissue sarcomas than any other racial/ethnic group.
- An epidemic of Kaposi sarcoma occurred in young adult males during the 1980s and early to mid-1990s as a result of the human immunodefciency virus (HIV) and the associated acquired immunodeficiency disorder syndrome (AIDS).
- At its peak incidence during the late 1980s and early 1990s, Kaposi sarcoma accounted for more cases of sarcoma in young adult males than any other type of sarcoma. Since 2000, Kaposi sarcoma has accounted for about 5% and < 0.5% of the soft tissue sarcomas in 15- to 29-year-old males and females, respectively.

Mortality & Survival

- In nearly all age categories, mortality for males with soft tissue sarcomas was higher than for females, with the exception of those in the 10- to 14-year age group, for whom survival was equal for both genders.
- Among those diagnosed during the past quarter century, 15- to 29-year-olds with non-Kaposi soft tissue sarcomas had the second highest survival rate, following that of those in the 30- to 44-year age bracket.
- Among those with rhabdomyosarcoma and embryonal sarcoma, 15- to 29-year-olds had both a lower survival rate and a less favorable survival improvement trend than children with these types of sarcoma.
- Racial/ethnic minority patients in the 15- to 29-year age group did not have, in general, an inferior outcome in survival for either non-Kaposi soft tissue sarcomas or Kaposi sarcoma; Asians/Pacific Islanders with Kaposi sarcoma who were diagnosed between 15 and 30 years of age were an exception.
- Kaposi sarcoma had the most dramatic increase in survival improvement among the major groups of soft tissue sarcomas, albeit it was still lower than for most types of soft tissue sarcomas.
- Those diagnosed with Kaposi sarcoma before age 30 had the worst survival and the least improvement in survival of all age groups.

Risk Factors

- Genetic disorders associated with an increased risk of soft tissue sarcomas are Li-Fraumeni Syndrome (LFS), von Recklinghausen's disease, and Beckwith-Wiedeman Syndrome (BWS).
- Environmental factors associated with an increased risk of rhabdomyosarcoma in children include fetal exposure to marijuana and cocaine use by the mother and/or father; it is unknown if this applies to those who develop rhabdomyosarcoma as adolescents and young adults.
- Survivors of soft tissue sarcomas, especially those who received multi-modal therapy, have a significantly increased risk for the development of second malignant neoplasms.

INTRODUCTION

Soft tissue sarcomas generally arise from malignant transformation of a mesenchymal cell of origin, which normally would mature into skeletal muscle, smooth muscle, fibrous tissue, adipose tissue, or cartilage. Current therapeutic options in the U.S. are based on

pathologic classification and other clinical and biologic characteristics, including chromosomal abnormalities.[1] This chapter will review SEER data for soft tissue sarcomas collectively as well as by specific pathologic type, by race/ethnicity, and by incidence, mortality, and survival from 1975 to 1999. Because the epidemic of Kaposi sarcoma in the U.S. occurred during the era that is the focus of this monograph, and predominantly affected young adult males, special sections on Kaposi sarcoma are presented in this chapter.

METHODS, CLASSIFICATION SYSTEM, AND BIOLOGICAL IMPLICATIONS

Soft tissue sarcomas in the International Classification of Childhood Cancer (ICCC) is Category IX. Subcategory IX(a) is rhabdomyosarcoma and embryonal sarcoma, IX(b) is fibrosarcoma, neurofibrosarcoma, and fibromatous neoplasms, IX(c) is Kaposi sarcoma, IX(d) is all other specified soft tissue sarcomas, and IX(e) is other and unspecified soft tissue sarcomas.

The *Rhabdomyosarcoma and Embryonal* sarcoma category IX(a) is composed of ICD-O-2 categories 8900-8920 (various forms of rhabdomyosarcoma) and 8991 (embryonal sarcoma). Also included but not shown in ICCC is rhabdomyosarcoma with ganglionic differentiation (ICD-O-3 8921).

The *Fibrosarcoma, Neurofibroma, and Fibromatous Neoplasm* category IX(b) is comprised of fibrosarcoma (8810), malignant fibrous histocytoma (8830), fibromyxoma and fibromyxosarcoma (8811), fascial fibrosarcoma (8813), malignant solitary fibrous tumor (8815), infantile fibrosarcoma (8814), dermatofibrosarcoma (8832), pigmented dermatofibrosarcoma protuberans (8833), and malignant peripheral nerve sheath tumors (9540-9561). The *Kaposi Sarcoma* category IX(c) is a single category in the ICD-O-2: 9140.

The *Other Specified Sarcoma* category IX(d) is constituted by a variety of neoplasms: extraosseous Ewing sarcoma (category 9260); peripheral neuroectodermal tumor (9364); synovial-like neoplasms (e.g. synovial sarcoma) (9040-9044); giant cell tumor of soft parts (9251); alveolar soft-part sarcoma (9581); malignant rhabdoid sarcoma (8963); myoepithelioma (8982); mesenchymoma (8990); blood vessel neoplasms (e.g. hemangioendotheloiomas, hemangiopericytoma) (9120-9134, 9150-9161); lymphatic-like neoplasms (e.g. lymphangiosarcoma) (9170); non-osseous myxoid chondrosarcoma (9231); non-osseous mesenchymal chondrosarcoma (9240), myxomatous, myomatous and lipomatous neoplasms (8840-8896), myxosarcoma (8840), various liposarcomas (8850-8881), and various leiomyosarcomas and myosarcomas (8890-8896). Also included but not shown in ICCC are specific histologies from ICD-O-3: undifferentiated sarcoma (8805) and desmoplastic small round cell tumor (8806). Because the gastrointestinal stromal tumors are considered benignor of borderline malignancy, they are not included in the analysis.

The *Unspecified Sarcoma* category IX(d) is constituted by soft tissue sarcoma NOS , spindle cell sarcoma (8801), non-osseous giant cell sarcoma (8802), small cell sarcoma (8803), and epithelioid sarcoma (8804). The female genital tract sarcomas (e.g. uterine leiomyosarcomas) are included in the *Unspecified Sarcoma* category of ICCC. Stromal sarcoma NOS (8930, and in ICD-O-3: 8930, 8935) is included in ICCC XII(a)

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

In attempting to apply the ICCC and SEER site recode to soft tissue sarcoma in 15- to 29-year-olds, it is apparent that the SEER site recode does not break down any of the specific sarcomas and the ICCC only uses sarcoma subgroups which would be seen among young children. Specific sarcomas which would be rare or non-existent among young children, such as leiomyosarcoma of the female genital tract, may be important for the 15- to 29-year-olds but are not shown separately in ICCC. A soft tissue sarcoma classification specific to this age group is needed.

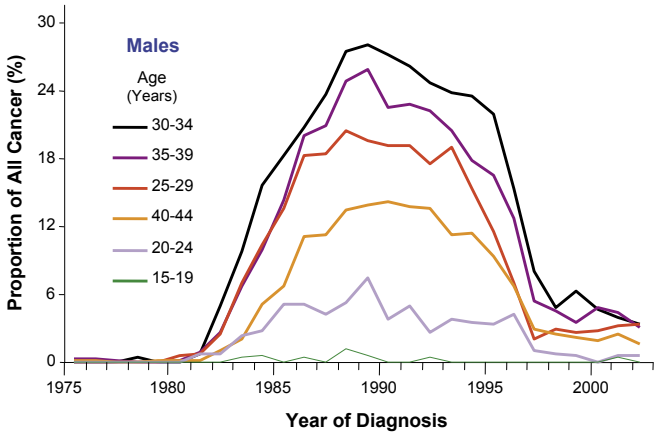

Figure 7.1: Proportion of All Invasive Cancer that was Kaposi Sarcoma, by Age, **Males**, SEER 1975-2002

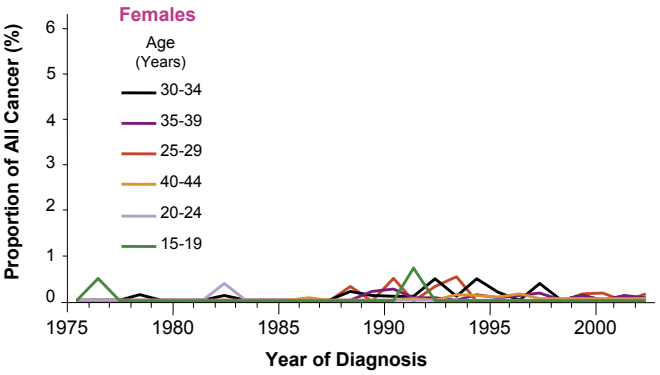

Figure 7.2: Proportion of All Invasive Cancer that was Kaposi Sarcoma, by Age, **Females**, SEER 1975-2002

INCIDENCE OF KAPOSI SARCOMA

In the U.S, the human immunodeficiency virus (HIV) epidemic of the 1980s led to an epidemic of AIDS-related Kaposi sarcoma in young adults males that peaked during 1986 to 1995 and subsided by the end of the 1990s (Figures 7.1 and 7.2).[2-4] In certain parts of the U.S, the increased incidence of Kaposi sarcoma in the early 1980s heralded the epidemic of HIV.[5] The age group most affected was 20- to 49-year-olds, with a peak in 30- to 34-year-olds, but cases in 15- to 19-year-olds were also reported. A few other cancers also increased during this interval, especially non-Hodgkin lymphoma (cf. *Introduction and Lymphoma* chapters), but no other cancer had as great an impact on the overall incidence of cancer in young adults.

The percent of all invasive cancers that was Kaposi sarcoma was as high as one in every four cancers in males who were 35 to 39 years of age (Figure 7.1). In 15- to 29-year-old males, the proportion peaked at 12%, and among 25- to 29-year-olds it peaked at 18%. Hence, Kaposi sarcoma had a profound effect on the incidence of cancer in young adult males up to end of the 1990s. This chapter therefore reviews soft tissue sarcomas during the era 1975 to 2000 era with and without Kaposi sarcoma.

INCIDENCE

Age-specific incidence

The incidence of both Kaposi sarcoma and the non-Kaposi soft tissue sarcomas were highly age-dependent.

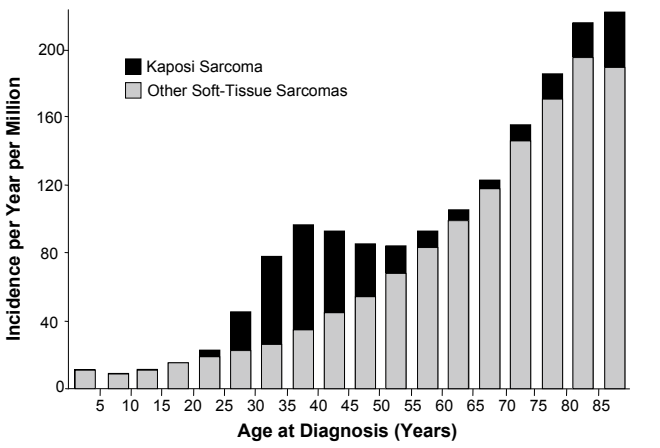

Figure 7.3: Incidence of All Soft Tissue Sarcomas, SEER 1975-2000

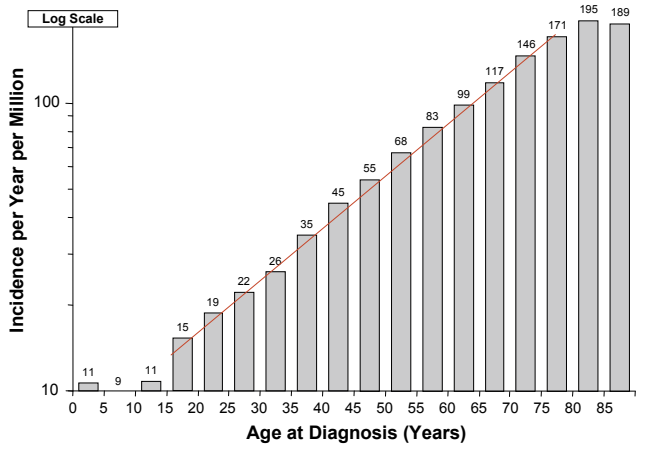

Figure 7.4: Incidence of Non-Kaposi Soft Tissue Sarcomas, SEER 1975-2000

Table 7.1: *Incidence of Soft Tissue Sarcomas 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 SOFT TISSUE SARCOMAS EXCLUDING KAPOSI						
Average incidence per million, 1975-2000, SEER	8.4	6.4	6.4	9.3	14.4	38.5
Average annual % change in incidence, 1975-2000, SEER	-0.4%	-0.5%	1.4%	-0.8%	2.4%	12.9%
Estimated incidence per million, year 2000, U.S.	8.2	6.2	7.3	8.2	17.9	62.3
Estimated number of persons diagnosed, year 2000, U.S.	156	127	150	165	339	1,207
FIROSARCOMA, NEUROFIBROSARCOMA, OTHER FIBROMATOSIS MALIGANCIES*						
Average incidence per million, 1975-2000, SEER	1.9	1.4	3.4	5.5	8.6	11.3
Average annual % change in incidence, 1975-2000, SEER	5.8%	9.1%	0.1%	-1.6%	0.5%	1.3%
Estimated incidence per million, year 2000 , U.S.	2.2	1.3	3.4	4.1	9.2	12.8
Estimated number of persons diagnosed, year 2000, U.S.	42	27	70	83	174	248
RHABDOMYOSARCOMA**						
Average incidence per million, 1975-2000, SEER	6.5	4.9	3.0	3.5	1.6	0.8
Average annual % change in incidence, 1975-2000, SEER	1.1%	-0.3%	3.6%	0.9%	-2.8%	^
Estimated incidence per million, year 2000, U.S.	7.3	4.7	3.8	3.9	0.5	^
Estimated number of persons diagnosed, year 2000, U.S.	140	96	78	79	10	^
KAPOSI SARCOMA***						
Average incidence per million, 1975-2000, SEER	0	0	0	0.2	4.0	25.2
Estimated incidence per million, year 2000, U.S.	0	0	0	0.1	0.9	7.5
Estimated number of persons diagnosed, year 2000, U.S.	0	0	0	^	17	145

***ICCC IX(b) **ICCC IX(a) ***ICCC IX(d) ^Too few for reliable estimate**

Whereas Kaposi sarcoma had a peak incidence in young adults during the era 1975 to 2000, the other soft tissue sarcomas did not (Figure 7.3). Between peaks in early childhood and in elderly persons, the incidence of non-Kaposi soft tissue sarcomas increased exponentially from 15 to 75 years of age (Figure 7.4).

From 1975 through 1999, the incidence of soft tissue sarcomas—excluding Kaposi sarcoma—dramatically increased among 15- to 29-year-olds as a function of age, from 9.3 per year per million among 15- to 19-year-olds to 38.5 per year per million 25- to 29-year-olds (Figure 7.5). The age-dependent incidence continued to increase until a peak among 35- to 39-year-olds and then declined among older persons (Figure 7.3). More than 40% of the non-Kaposi soft tissue sarcoma cases occurred in 25- to 29-year-olds.

During the period 1975 to 1999, non-Kaposi soft tissue sarcomas comprised approximately 4-7% of all invasive cancer in the 15- to 29-year age group (Figure 7.5 inset). Excluding Kaposi sarcoma, soft tissue sarcomas peaked as a proportion of all cancer between 25 and 35 years of age, with a maximum of 9% occurring in 30- to 34-year-olds (Figure 7.5).

By the year 2000, when the Kaposi sarcoma epidemic had all but subsided (Figure 7.1), the total number of soft tissue sarcomas diagnosed in the U.S. in 15- to 29-year-olds was approximately 1,875, based on incidence trends over the prior 25 years and on age- and year-specific population (Table 7.1). About 1,700 15- to 29-year-olds were diagnosed in the year 2000 with non-Kaposi soft tissue sarcoma and 160 persons in the age group had Kaposi sarcoma. Approximately 165 of these cases were observed in 15- to 19-year olds, 360 in 20- to 24-year olds, and 1,350 in the 25- to 29-year age group (Table 7.1). The ICCC group of fibrosarcomas and related fibromatous entities constituted the largest histologic group of sarcomas

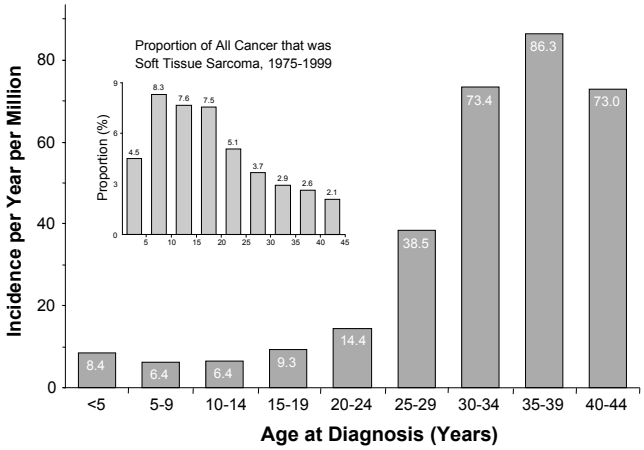

Figure 7.5: Incidence of Soft Tissue Sarcomas excluding Kaposi Sarcoma, SEER 1975-1999

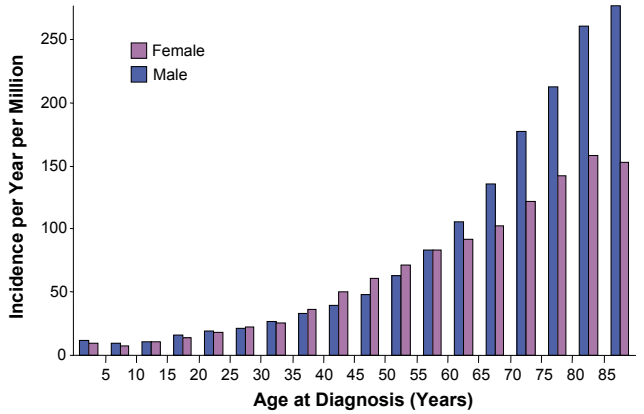

Figure 7.6: Incidence of Non-Kaposi Soft Tissue Sarcomas by Gender, SEER 1975-2000

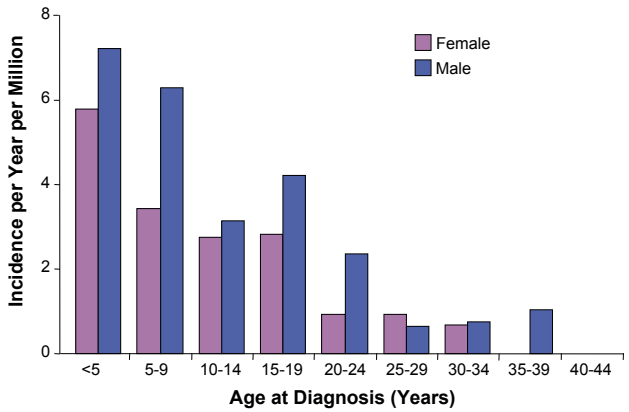

Figure 7.7: Incidence of Rhabdomyosarcoma by Gender, SEER 1975-1999

among 15- to 29-year-olds, accounting for 30% of non-Kaposi soft tissue sarcomas in the year 2000 (Table 7.1).

Histology-specific incidence

One contrast between sarcomas in the 15- to 29-year age group in comparison to those that occurred before age 15 was the much larger variety of histologic types. From 1992 to 2002, during which the Kaposi sarcoma epidemic subsided, there were a dozen histologic types accounting for 1% to 15% of the soft tissue sarcomas (Table 7.2). Rhabdomyosarcoma and other embryonal sarcomas, derived from mesenchymal cells of striated muscle origin,[6] predominated in those younger than age 15. Many connective tissues cells of non-muscle-origin contributed to the sarcomas that arose in 15- to 29-year-olds, including those of fibrous, neuroectodermal, vascular, adiopose, cartilage and synovial origin.

Gender-specific incidence

Except during middle age (35 to 55 years), males had a higher incidence of non-Kaposi soft tissue sarcoma (Figure 7.6). The male predominance was small among children, adolescents and young adults, but much greater, nearly two-fold, among older adults. Although uterine leiomyosarcomas and other genital tract sarcomas were included among the female sarcomas, they accounted for few of the sarcomas that occurred between 15 and 30 years of age.

In almost all age categories, males had a higher incidence of rhabdomyosarcoma when gender-specific incidence

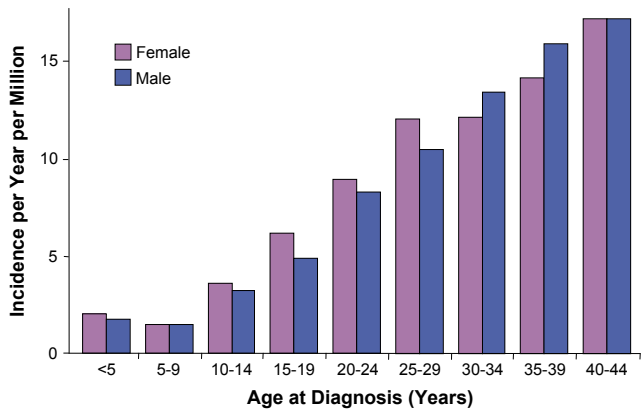

Figure 7.8: Incidence of Fibrosarcoma, Neurofibrosarcoma, and Other Fibromatous Neoplasms by Gender, SEER 1975-1999

patterns were calculated. Only in the 25- to 29-year age group was incidence in females greater than that in males (Figure 7.7). The pattern of higher incidence rates for males did not, however, persist for fibrosarcoma, neurofibrosarcoma and other fibromatous neoplasms (Figure 7.8).

In 15- to 29-year-olds, the majority of soft tissue sarcomas occurred in the trunk, head/neck and extremities (Figure 7.9). The order of frequency by anatomic location was trunk, leg, head, neck and arm/shoulder. The anatomic distribution was remarkably similar in males and females, even when uterine and other female genital tract sarcomas were included.

Racial/Ethnic Differences in Incidence

African Americans/blacks from age 10 to 45 had a higher incidence of non-Kaposi soft tissue sarcomas than any other racial/ethnic group (Figure 7.10). [They also had a higher incidence of Kaposi sarcoma]. Non-Hispanic whites, Hispanics, Asians/Pacific Islanders and American Indians/Alaska Natives generally followed in incidence. American Indians/Alaska Natives 20 years of age and older had one-half the incidence, on average, of African Americans/blacks.

Histology-Specific Incidence by Race/Ethnicity

African Americans/blacks had the highest incidence of rhabdomyosarcoma and embryonal sarcomas in the 15- to 29-year age group and Asians/Pacific Islanders had the

Table 7.2: *Soft Tissue Sarcomas by Histologic Type in 15- to 29-Year-Olds, 1992-2002*

HISTOLOGIC TYPE	% OF TOTAL
Kaposi Sarcoma	35.3%
Dermatofibrosarcoma, including protuberans	14.9%
Leiomyosarcoma, Fibrosarcoma	6.3%
Rhabdomyosarcoma	6.5%
Synovial Cell Sarcoma	6.0%
Ewing Sarcoma / PNET	4.8%
Malignant Fibrous Histiocytoma	4.3%
Liposarcoma	4.3%
Malignant Peripheral Nerve Sheath Tumor	3.8%
Angiomatous / Vascular Sarcomas	2.3%
Spindle Cell Sarcoma	1.5%
Epithelioid Sarcoma	1.4%
Alveolar Soft Part Sarcoma	1.2%
Clear Cell Sarcoma	1.0%
Small Cell Sarcoma	0.6%
Chondrosarcoma (Soft Tissue)	0.5%
Giant Cell Sarcoma	0.4%
Desmoplastic Small Round Cell Tumor	0.4%
Miscellaneous	4.5%
Total Number	**2812**

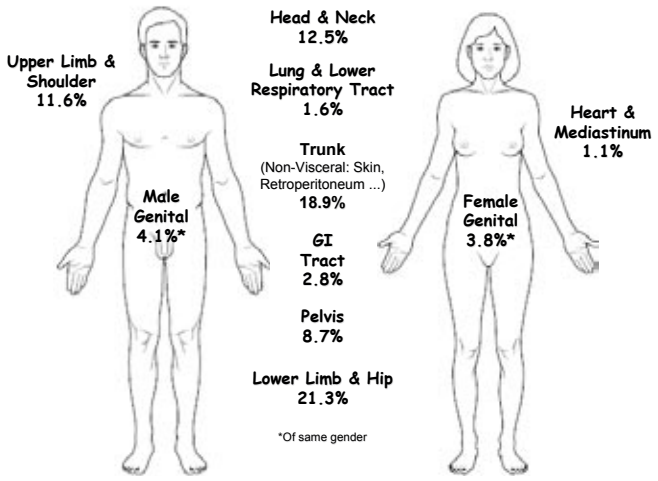

Figure 7.9: Percentage of Soft Tissue Sarcomas by Location for Age 15 to 29, SEER 1992-2002. Drawings by Medscape

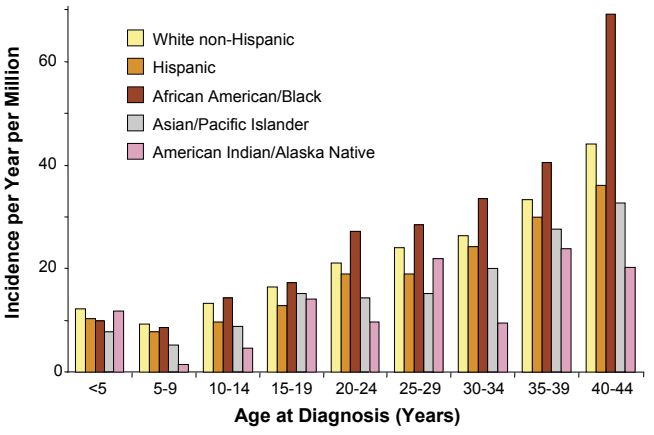

Figure 7.10: Incidence of Non-Kaposi Soft Tissue Sarcomas by Race/Ethnicity, SEER 1992-2002

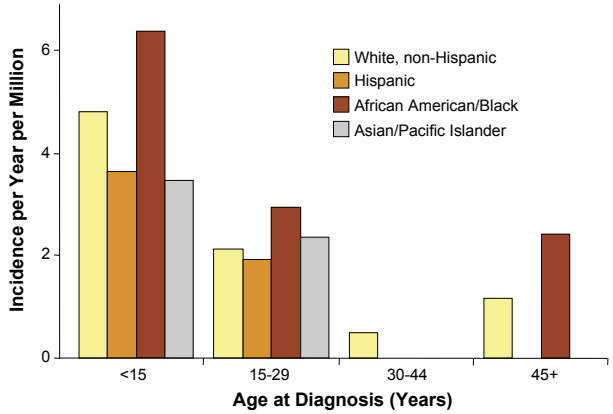

Figure 7.11: Incidence of Rhabdomyosarcoma and Embryonal Sarcoma by Race/Ethnicity, SEER 1990-1999

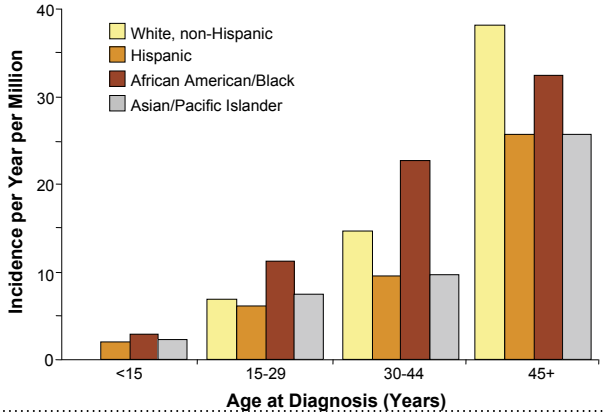

Figure 7.12: Incidence of Fibrosarcoma, Neurofibrosarcoma, and Other Fibromatous Neoplasms by Race/Ethnicity, SEER 1990-1999

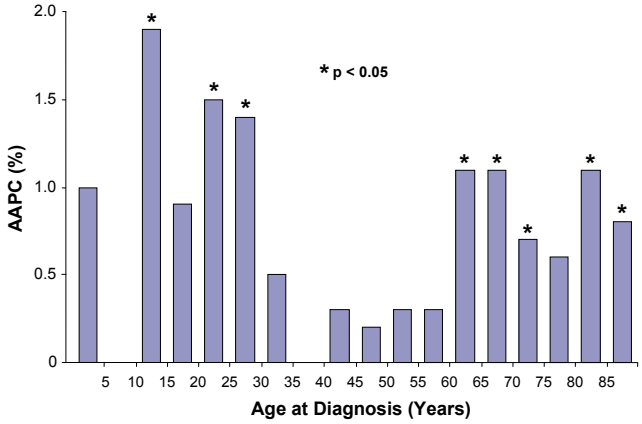

Figure 7.13: Average Annual Percent Change (AAPC) in Incidence of Non-Kaposi Soft Tissue Sarcoma, SEER 1975-2000

second highest incidence (Figure 7.10). White non-Hispanics and Hispanics had a similar incidence. Incidence of rhabdomyosarcoma and embryonal sarcoma was quite low in those 30 to 44 years of age; white non-Hispanics were the only group with enough cases to analyze (Figure 7.11). Interestingly, once over the age of 45, white non-Hispanics and African Americans had an incidence similar to, although lower than, these same groups at 15 to 29 years of age.

Variations in incidence when stratified by race/ethnicity in the adult population have also been reported. An analysis of SEER data from 1973 to 1998 for *primary upper-extremity* soft tissue sarcomas found that whites had a higher incidence when compared to African Americans/blacks.[7] A retrospective cohort analysis of children treated on the Intergroup Rhabdomyosarcoma Study Group protocols between 1984 and 1997 revealed that patients from ethnic minority groups presented with larger, more invasive tumors with positive lymph nodes.[8]

For fibrosarcoma, neurofibrosarcoma, and other fibromatous neoplasms, the incidence patterns by race/ethnicity were similar to those observed in aggregate for all soft tissue sarcomas. Specifically, African Americans/blacks had the highest incidence of those younger than 45 years of age. White non-Hispanics had the second highest incidence in this age range, but the highest incidence in persons over 45 years of age (Figure 7.12).

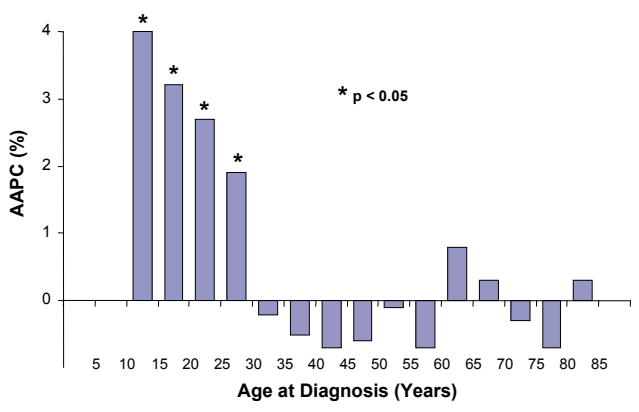

Figure 7.14: Average Annual Percent Change (AAPC) in Incidence of Other Specified Soft Tissue Sarcoma, ICCC IX(d), SEER 1975-2000

Trends in Incidence

From 1975 to 2000, non-Kaposi soft tissue sarcoma increased at a statistically significant rate in 10- to 29-year-olds and in persons over 60 (Figure 7.13). The increase was primarily due to sarcomas in the *Other Specified soft tissue sarcoma* ICCC group IX(d) (Figure 7.14) that includes extra-osseous Ewing sarcoma, peripheral neuroectodermal tumor, and synovial-cell sarcoma.

The increase in non-Kaposi soft tissue sarcomas was apparent in both males and females, but was greater in females and greater in the 15- to 29-year age group than in any other (Figure 7.15; left panel). The *Other Specified soft tissue sarcoma* group was the main contributor to both the male and female increases, and again was greater in 15- to 29-year-olds for both genders than in any other age group (Figure 7.15; right panel).

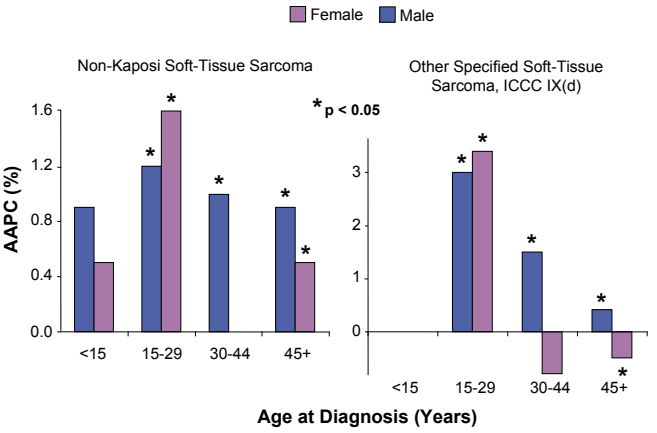

Figure 7.15: Average Annual Percent Change (AAPC) in Incidence by Gender, SEER 1975- 2000

OUTCOME

Mortality

Note: Kaposi sarcoma was not separated from the other soft tissue sarcomas for mortality assessment and trends since this information was generally not available from death certificates until 1999. Even after 1999, deaths were not assigned to Kaposi Sarcoma but to AIDS *and* Kaposi Sarcoma.

Age-and Gender-Specific Mortality

National mortality for all soft tissue sarcomas from 1975 to 1999 showed a steady increase with age, from less than 2 deaths per million for both males and females younger than five years of age to a peak of 9 deaths per million for males 40 to 44 years of age. In most age categories—except the 10- to 14-year age group—mortality for males was greater than for females (Figure 7.16).

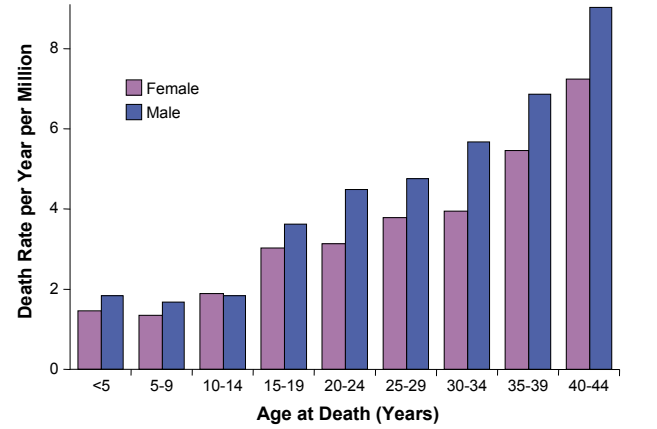

Figure 7.16: National Mortality for All Soft Tissue Sarcomas by Gender, U.S.,1975-1999

Racial/Ethnic Differences in Mortality

When mortality data were analyzed according to race/ethnicity, African Americans/blacks had the highest number of deaths per year per million in all age categories (Figures 7.17 and 7.18). The highest annual death rate was observed in the 40- to 44-year age group, at 13 deaths per million for African Americans/blacks, followed by 8 deaths per million for white non-Hispanics, 7

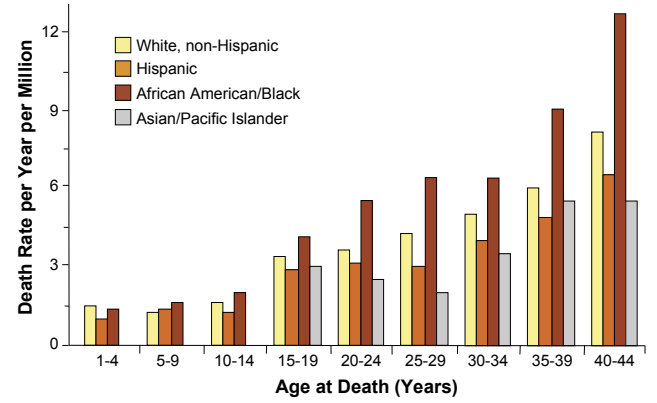

Figure 7.17: National Mortality for All Soft Tissue Sarcomas by Race/Ethnicity, 1990-2000

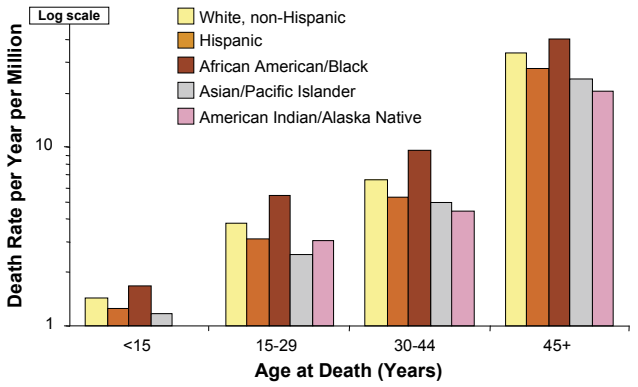

Figure 7.18: National Mortality for All Soft Tissue Sarcomas by Race/Ethnicity, U.S., 1990-2000

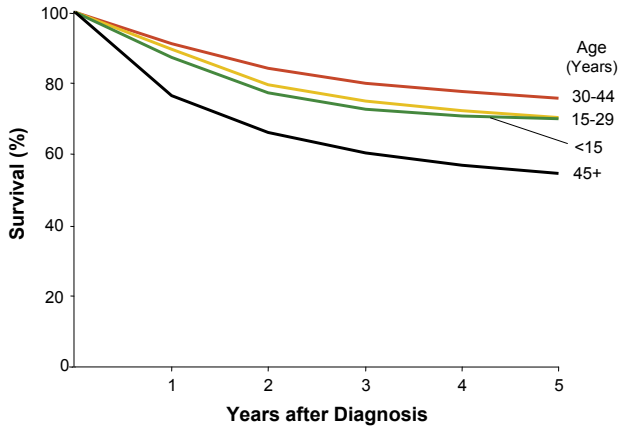

Figure 7.19: Relative Survival Rate for Non-Kaposi Soft Tissue Sarcoma by Age, SEER 1975-2000

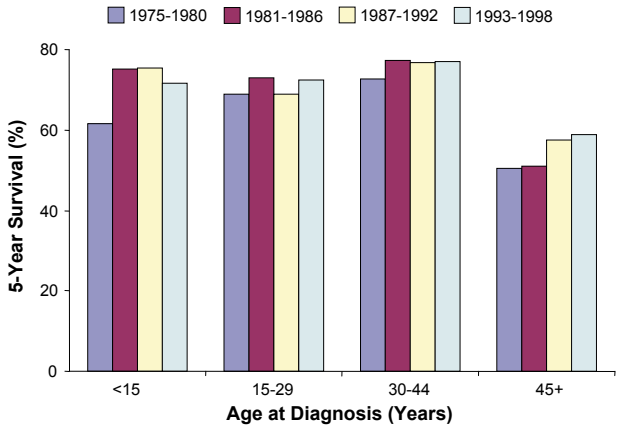

Figure 7.20: 5-Year Survival Rate for Non-Kaposi Soft Tissue Sarcomas by Era, SEER

deaths per million for Hispanics, and 6 deaths per million for Asians/Pacific Islanders (Figure 7.18).

Survival

Life table analysis disclosed that between 1975 and 2000, children, adolescents and young adults with non-Kaposi soft tissue sarcomas had a better than 75% relative survival (Figure 7.19). Those 30 to 44 years of age had the best outcome—approximately 80% at 5 years—and those in the 15- to 29-year age group had the next best outcome. Even in children, age has been reported to be an independent prognostic factor for treatment failure: children with rhabdomyosarcoma who are younger than one year of age or older than ten years have a poor outcome.[8]

Little-to-no progress was made during the past quarter century in prolonging the survival of patients with non-Kaposi soft tissue sarcomas in the 15- to 29-year age groups (Figure 7.20). Younger and older patients have had lives prolonged, particularly those over 45 years of age.

It has been shown that patients with unresectable tumors and/or metastatic disease have a very poor long-term prognosis, and recent studies have shown that certain genetic markers can affect prognosis.[9] However, cytogenetics of the various soft tissue sarcomas and staging of the individuals represented in the adolescent and young adult cohort are not known.

When survival rates for rhabdomyosarcoma and embryonal sarcoma were analyzed by treatment eras, only those younger than 15 years of age showed an improvement in survival over time. The 5-year survival rates for adolescents and young adults were low—approximately 40%—throughout all treatment eras. Survival rates for those in the 30- to 44-year age group decreased from approximately 42% in the early treatment eras to under 20% in the most recent treatment era, and as discussed above, were primarily due to the HIV epidemic and the associated occurrence of Kaposi sarcoma. The survival rates remained constant, although low at approximately 30%, for those 45 years and older (Figure 7.21).

Five-year survival rates for fibrosarcomas, neurofibrosarcomas and other fibromatous neoplasms were nearly 90% for all age groups from 15 to 44 years. The survival rate

for the 45 and older age group was not quite as high but reached a maximum of approximately 75% in the most recent treatment era (Figure 7.22).

When evaluating the average annual percent change in 5-year survival for all soft tissue sarcomas over the period 1975 to 1997, a decrease in survival is noted in all age groups between 15 and 44 years. These findings have also been observed in a recent study that reported the lowest survival improvement in those between the ages of 15 and 45 years, with the exception of Kaposi sarcoma.[10] Furthermore, the study found that age-dependent survival improvement and clinical-trial accrual patterns were directly correlated ($p < 0.005$). This suggests that the lack of survival improvement in persons between the ages of 15 and 44 years in the U.S. with non-Kaposi sarcomas may have been a result of limited participation in clinical trials (Figure 7.23).[10]

Survival by Race/Ethnicity

Small variations in 5-year survival rates for all soft tissue sarcomas were noted among the different racial/ethnic groups (Figure 7.24). For adolescents and young adults, Hispanics and white non-Hispanics demonstrated the highest survival rates, at approximately 80%, followed closely by African Americans/blacks and Asians/Pacific Islanders, with survival rates of approximately 75%. For adults in the 30- to 44-year age group, survival was almost 90% for white non-Hispanics, 85% for Hispanics and African Americans/blacks and 77% for Asians/

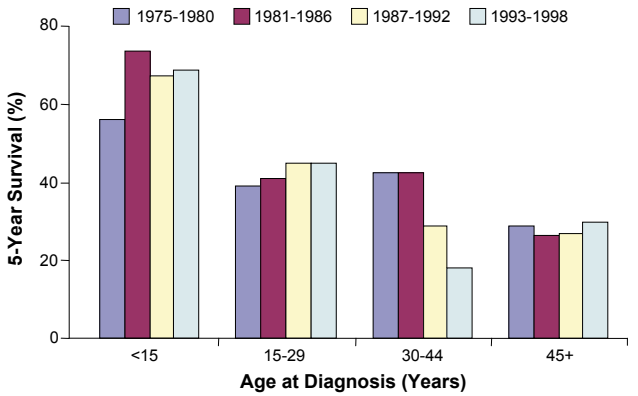

Figure 7.21: 5-Year Survival Rate for Rhabdomyosarcoma and Embryonal Sarcoma, ICCC IX(a), by Era, SEER

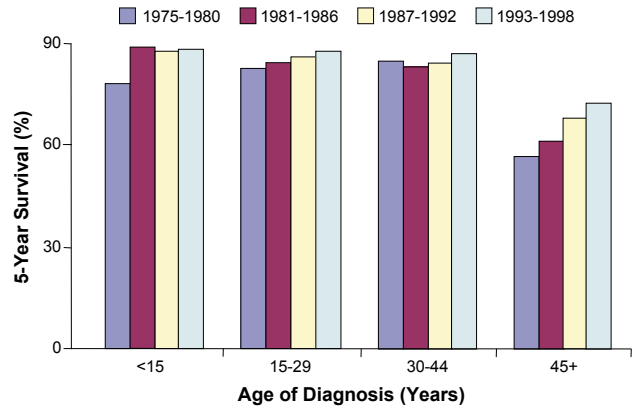

Figure 7.22: 5-Year Survival Rate for Fibrosarcoma, Neurofibrosarcoma and Other Fibromatous Neoplasms, ICCC IX(b), by Era, SEER

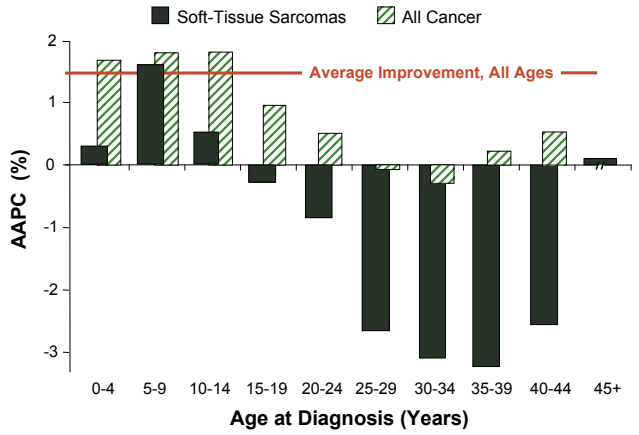

Figure 7.23: Average Annual Percent Change (AAPC) in 5-Year Survival, 1975-1997

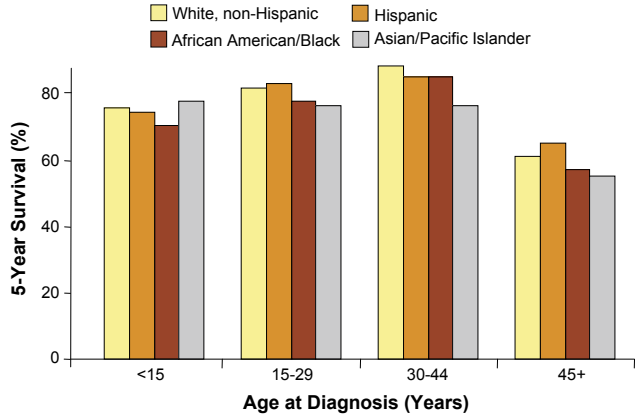

Figure 7.24: 5-Year Survival Rate for All Soft Tissue Sarcomas by Race/Ethnicity, SEER 1990-1999

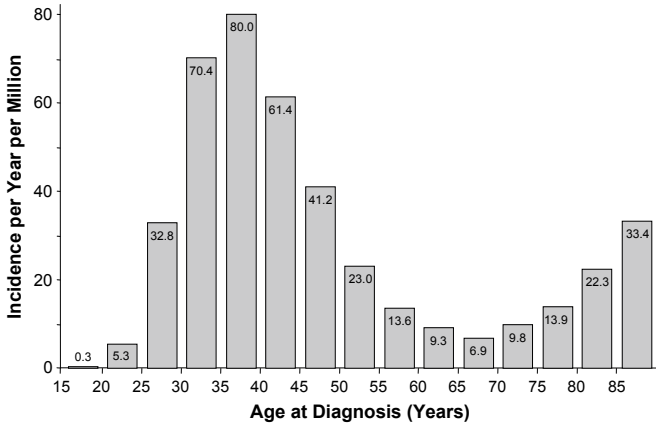

Figure 7.25: Incidence of Kaposi Sarcoma, SEER 1983-2002

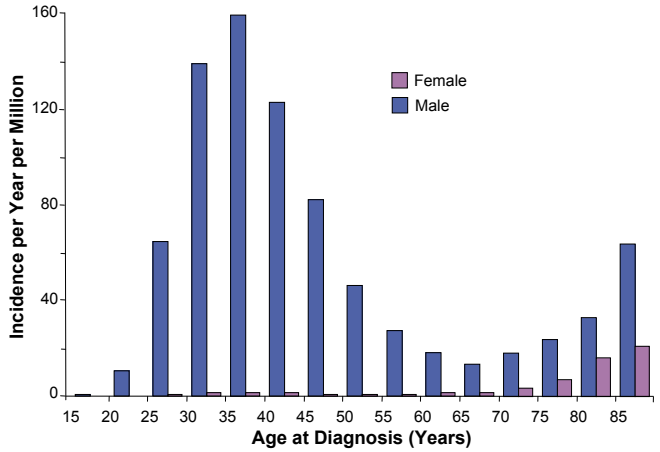

Figure 7.26: Incidence of Kaposi Sarcoma by Gender, SEER 1983-2002

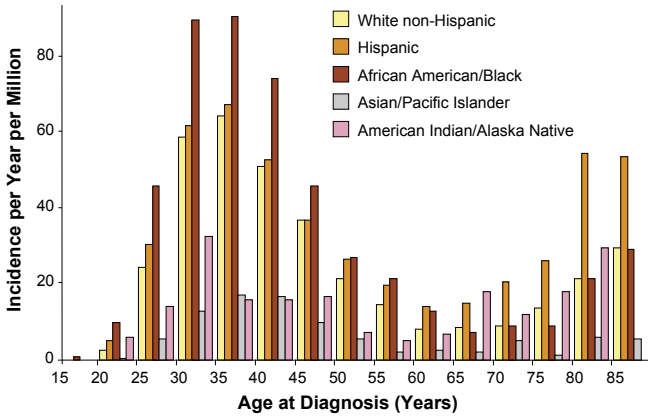

Figure 7.27: Incidence of Kaposi Sarcoma by Age and Race/Ethnicity, SEER 1992-2002

Pacific Islanders. The lowest survival rates occurred for those over 45 years of age, and were between 58% and 62% for all groups.

KAPOSI SARCOMA

Incidence

As mentioned at the beginning of this chapter, the dramatic increase and decline of Kaposi sarcoma among young males during the 1980s and 1990s (Figure 7.1) requires that this disease be considered separately when describing the history of sarcoma epidemiology during the past quarter century. There was a bimodal distribution of incidence as a function of age, with the young adult peak occurring between 35 and 40 years of age and a peak occurring in the elderly after 85 years of age (Figure 7.25). The youngest age group with a measurable rate was 15 to 19 years. Nearly all cases in young adults have occurred in males; females, however, had an increasing incidence after age 60 and approached one-third to one-half the male incidence after age 80 (Figure 7.26).

During the latter half of the Kaposi epidemic, when race and ethnicity were ascertained by the U.S. Census Bureau, African Amercans/blacks had the highest incidence of Kaposi sarcoma in all ages up to 60 years (Figure 7.27). In elderly persons, Hispanics had the highest incidence, approximately twice that of other races/ethnicities. In young adults, non-Hispanic whites and Hispanics had similar rates of Kaposi sarcoma. The lowest rates occurred in Asians/Pacific Islanders, and American Indians/Alaska Natives had intermediate rates.

Survival

Historically, 15- to 29-year-olds with Kaposi sarcoma had the same poor survival—15% at 5 years—as those 30 to 44 years of age, and both of these age groups had a distinctly worse outcome than those 45 years of age and older (Figure 7.28). Historically, the two races with the highest incidence of Kaposi sarcoma in 15- to 29-year-olds—African Americans/blacks and whites—had nearly identical survival rates (Figure 7.29). Both races experienced a doubling in 5-year survival rates, albeit the 1-year survival rate among African Amercans/blacks lagged behind that of whites (Figure 7.28).

The 5-year survival among young adults with Kaposi sarcoma declined before it improved, however, with the 1987 to 1992 era having the worst outcome in all age groups (Figure 7.30). This decline across all age groups is unexplained. It is unlikely to have been due to the HIV epidemic, since HIV-related Kaposi sarcoma occurred during the prior era—1981 to 1986—and because persons older than those who developed AIDS (the 45+ year age group), were similarly affected (Figure 7.30). Since then, however, remarkable progress has been made in prolonging survival. The age group with the least improvement in the 5-year survival rate was the 15- to 29-year-old group (Figure 7.30); those in the 20- to 24-year age group had a deterioration in survival from the survival rate of the early 1980s (Figure 7.31).

Among 15- to 29-year-olds, Asians/Pacific Islanders had the worst survival during the most recent era, 1992 to 1999. Their 5-year rate was 6% compared to 16-23% for the other racial/ethnic groups (Figure 7.32). Hispanic patients had the best survival among 30- to 44-year-olds, and non-Hispanic whites and African Americans/blacks had the best outcome of those 45 years of age and older.

RISK FACTORS

There are reports in the pediatric literature documenting that certain syndromes with known chromosomal abnormalities place children at risk for the development of soft tissue sarcomas. It should also be noted, however, that the majority of cases of soft tissue sarcomas occur sporadically, with no identifiable risk factor. Three genetic disorders associated with an increased incidence of soft tissue sarcomas are Li-Fraumeni Syndrome (LFS), von Recklinghausen's disease, and Beckwith-Wiedeman Syndrome (BWS). LFS has been associated with soft tissue sarcomas in children and the early onset of breast cancer in adult family members. This heterogeneous familial cancer syndrome is most notably associated with germline mutations in the p53 tumor suppressor gene, but other genetic abnormalities have also been noted.[11] There is an increased incidence of soft tissue sarcomas in patients with von Recklinghausen's disease, which is associated with abnormalities at the 17q11.2 locus.[12,13] Rhabdomyosarcoma has also been reported to have a higher incidence in children with Beckwith-Wiedeman

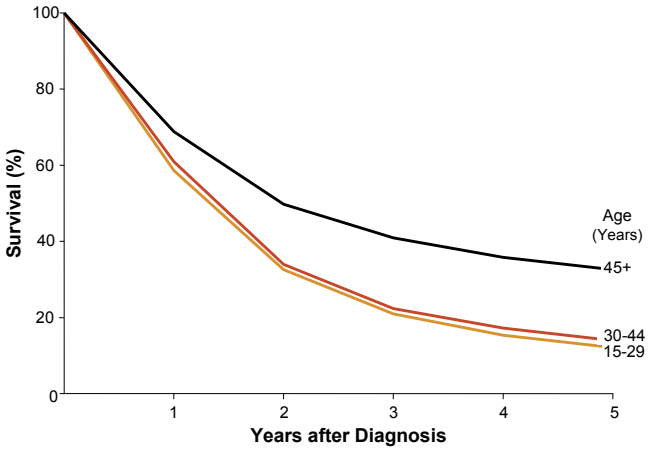

Figure 7.28: Relative Survival Rate for Kaposi Sarcoma by Age, SEER 1975-2000

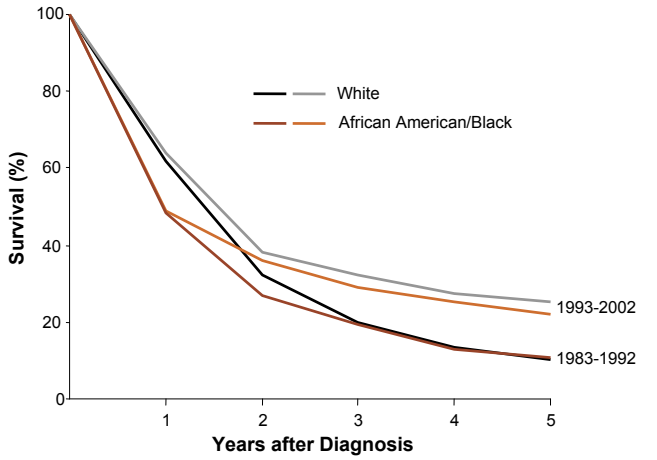

Figure 7.29: Relative Survival Rate for Kaposi Sarcoma by Era and Race, Age 15-29 at Diagnosis, SEERSEER 1981-1999

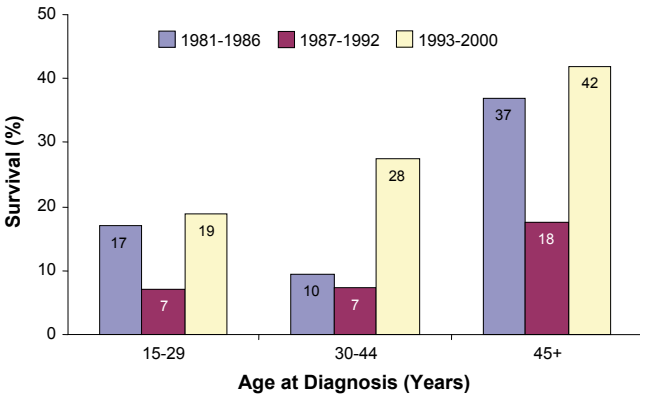

Figure 7.30: 5-Year Relative Survival Rate for Kaposi Sarcoma by Age and Era, SEER 1981-1999

Syndrome (BWS), a fetal overgrowth syndrome. BWS is associated with abnormalities on 11p15.[14]

Environmental factors that have been associated with an increased risk of rhabdomyosarcoma in children include fetal exposure to marijuana and cocaine use by the mother and/or father.[15] Whether or not this applies to adolescents and young adults with rhabdomyosarcoma is not known. It is also important to recognize that for *survivors* of childhood soft tissue sarcomas, there is a significantly increased risk for the development of second malignant neoplasms for all histologic types; this appears to be greatest among patients who received combination multi-modal therapy including ionizing radiation and chemotherapy,[16] and with combination chemotherapy.

SUMMARY

From 1975 through 1999, approximately 15 cases per year per million of soft tissue sarcomas (including Kaposi sarcoma) were diagnosed in 15- to 19-year-olds, approximately 25 cases per year per million were diagnosed in 20- to 24-year-olds, and nearly 50 cases per year per million were diagnosed in 25- to 29-year-olds. Soft tissue sarcoma incidence reached its peak in 35- to 39-year-olds, at 125 per year per million. There were different incidence patterns for the various histological subtypes for the older and younger age groups represented in this sample. One such difference included a higher incidence—up to 7 per year per million cases of rhabdomyosarcoma and other embryonal sarcomas—for those younger than 20 years of age, but a lower incidence—approximately one per year per million—for those older than 20 years. At its peak incidence, during the late 1980s and early 1990s, Kaposi sarcoma accounted for more cases of sarcoma in young adult males than any other type of sarcoma. Since 2000, Kaposi sarcoma accounted for about 5% and < 0.5% of the soft tissue sarcomas in 15- to 29-year-old males and females, respectively.

Differences in gender-specific incidence rates for soft tissue sarcomas were also observed. In those 20 years of age and older, male incidence was much higher than that of females. Incidence variations were also observed among the different racial/ethnic groups. For almost all age categories, African Americans/blacks had the highest incidence overall for soft tissue sarcomas. Fortunately, racial/ethic minority patients in the 15- to 29-year age group have not had, in general, an inferior outcome in survival, as has been similarly observed for children with the most common sarcoma in their age group.[17] This equity is true for both Kaposi sarcoma, with the notable exception of Asian/Pacific Islander patients, and non-Kaposi soft tissue sarcomas.

Among Americans diagnosed with non-Kaposi soft tissue sarcoma during the past quarter century, 15- to 29-year-olds had the second highest survival rate, following that of those in the 30- to 44-year age bracket. Among those with rhabdomyosarcoma and embryonal sarcoma, however, 15- to 29-year-olds had both a lower survival rate and a less favorable survival improvement trend than children with these types of sarcomas. With the possible exception of Asians with Kaposi sarcoma, racial/ethnic minority patients in the 15- to 29-year age group have not

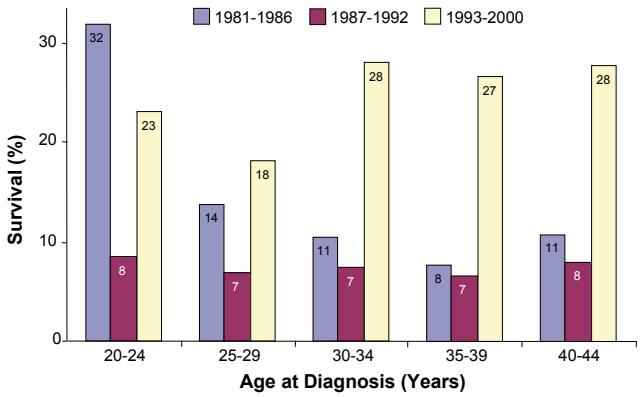

Figure 7.31: 5-Year Relative Survival Rate for Kaposi Sarcoma by Age and Era SEER 1981-1999

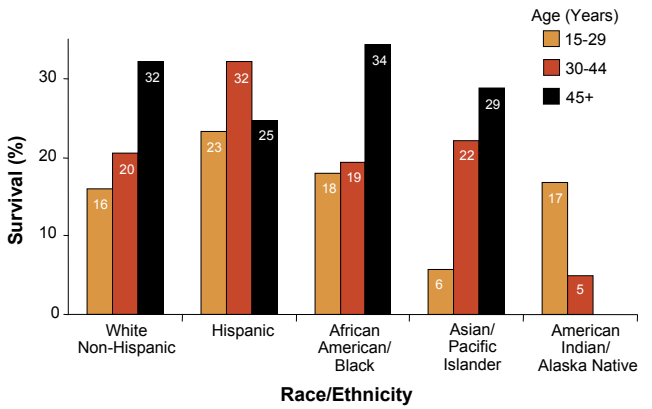

Figure 7.32: 5-Year Relative Survival Rate for Kaposi Sarcoma by Race/Ethnicity and Age, SEER 1992-1999

had an inferior outcome in survival of either non-Kaposi soft tissue sarcoma or Kaposi sarcoma.

Kaposi sarcoma had the most dramatic increase in survival improvement among the major groups of soft tissue sarcomas, albeit it was still lower than most types of soft tissue sarcomas. Those diagnosed with Kaposi sarcoma before age 30 had the worst survival and the least improvement in survival of all age groups.

The relative lack of progress in prolonging the lives of young adults with sarcomas has been correlated with the degree to which the disease has been studied in the age group (clinical trials, number of patients entered, etc.).[10] It is important to continue careful surveillance of soft tissue sarcoma survivors, considering their elevated risk for second malignant neoplasms, particularly if exposed to multi-modal treatment regimens.

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