RESEARCH ARTICLE

Age-Standardized Incidence Rates and Survival of Osteosarcoma in Northern Thailand

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Abstract

Osteosarcoma is a common primary malignant bone tumor in children and adolescents. Recent worldwide average incidences of osteosarcoma in people aged 0 to 24 years were 4.3 and 3.4 per million, respectively, with a ratio of 1.4:1. However, data on the incidence of osteosarcoma in Thailand are limited. This study analyzed the incidence of osteosarcoma in the upper northern region of Thailand, with a population of 5.85 million people (8.9% of the total Thai population), using data for the years 1998 to 2012, obtained from the Chiang Mai Cancer Registry (CMCR) at Chiang Mai University Hospital and the Lampang Cancer Registry (LCR) at the Lampang Cancer Hospital, a total of 144 cases. The overall annual incidence of osteosarcoma was 1.67 per million with a male:female ratio of 1.36:1. Incidences by age group (male and female) at 0 to 24, 25 to 59 and over 60 years were 3.5 (3.9 and 3.0), 0.8 (0.9 and 0.6), and 0.7 (0.8 and 0.5), respectively. The peak incidence occurred at 15 to 19 years for males and at 10 to 14 years for females. The median survival time was 18 months with a 5-year survival rate of 43%. Neither the age group nor the 5-year interval period of treatment was significantly correlated with survival during the 15-year period studied.

Keywords: Osteosarcoma - incidence rate - survival rate - epidemiology - gender - Thailand

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Introduction

Osteosarcoma, a common primary malignant bone tumor in children and adolescents (Settakorn et al., 2006; Damron et al., 2007), is one of the most aggressive human cancers and is the most common cause of cancer-associated limb loss (Settakorn et al., 2005). This cancer has a bimodal distribution, appearing more frequently in youth (age 0 to 24 years) and in the elderly (age more than 60 years) (Parkin et al., 1988; Damron et al., 2007; Mirabello et al., 2009a). Worldwide, the average incidence rate of osteosarcoma in youth (age 0 to 24 years) was 4.3 per million in males, and 3.4 per million in females, with a male to female ratio of 1.4:1. Females presented a peak incidence at a younger age than males (Mirabello et al., 2009a). In the elderly (age more than 60 years), the incidence rates of osteosarcoma were 4.0 per million in males and 3.1 per million in females. Strikingly higher rates were found in Australia, Canada, and UK (Mirabello et al., 2009a). Mirabello et al. reported that 35% of elderly osteosarcomas in the US were secondary to Paget disease of bone (Mirabello et al., 2009b).

A previous study of Thai people, however, noted that 85.7% of osteosarcomas occurred within the first three decades of life, with no significant bimodal age distribution. Gender distribution was in keeping with the rest of the world (Settakorn et al., 2007). Survival status and clinical outcomes of osteosarcoma treatment in Thailand have been reported in several studies of single institutes (Pochanugool et al., 1997; Arpornchayanon et al., 2011; Choeyprasert et al., 2013; Choeyprasert et al., 2014). However, there is only limited data on the incidence of the disease in a population-based study. Previous reports of incidence have covered only a small geographic area (Mirabello et al., 2009a; Wiromrat et al., 2012). This study reports the incidence, demographic data, and survival rate of osteosarcoma patients in a large geographic area of Northern Thailand with a population of 5.85 million people (8.9% of Thai population).

Materials and Methods

Data sources

Osteosarcoma cases were identified systematically from the Chiang Mai Cancer Registry (CMCR) and the Lampang Cancer Registry (LCR), between 1st January

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Table 1. Population-based Studies of Osteosarcoma Incidence Rates in Thailand

Author	Area	Baseline population	Age range	Period	Number of cases	M:F ratio	Age standardized incidence rate (cases/million/year)									
							overall	0 to 4	5 to 9	10 to 14	15 to 19	0 to 24		25 to 59		> 60	
												M	F	M	F	M	F
Current study	Upper North	5.9 Million	All range	1998-2012	144	1.36:1	1.67	0	2.5	5.4	6.6	3.9	3	0.9	0.8	0.8	0.5
Wiangnon et al 2011	Thailand	13.4 million	0-15 year	2003-2005	76	1.4:1	1.6	0.3	1.4	3.7							
Mirabello et al 2009a	Chiang Mai	1.59 Million	All range	1983-1997	36							3.8	1.2	1.6	0.2	2.1	0
Wiromrat et al 2012	Khon Khen	1.76 Million	0-19 years	1985-2010	58	1:1	3.1	0.3	1.2	4.1	8						

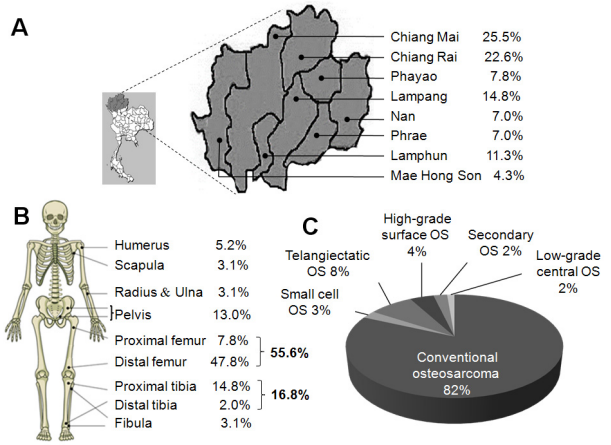

Figure 1. Demographic data on Osteosarcoma (OS) in the Northern Thai Region. Distribution of cases is categorized by province (A), anatomical location of the disease (B), and cellular subtype of osteosarcoma (C)

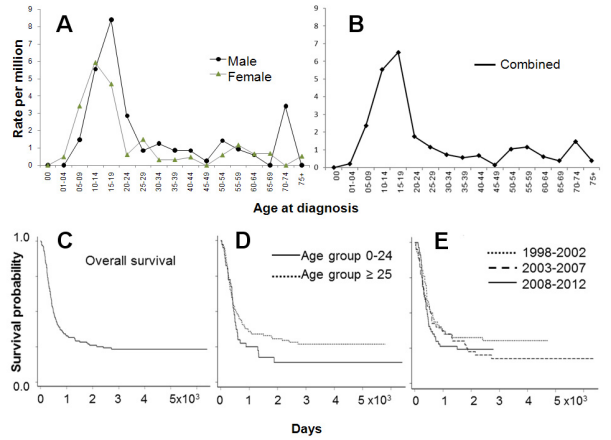

Figure 2. Age-adjusted Incidence of Osteosarcoma Categorized By Gender. (A), overall incidence (B), Kaplan-Meier curve of overall survival of osteosarcoma (C), survival rate categorized by age group (0-24 and >25 years) (D), and 5-year periods of treatment (E)

1998 to 31st December 2012. CMCR had registered all new cancer patients in Chiang Mai province while the LCR had registered all new cancer patients in the upper north region of Thailand except Chiang Mai province (the seven provinces of Chiang Rai, Mae Hong Son, Lampang, Lamphun, Phayao, Nan and Phrae). The population of the eight northern Thai provinces is 5.85 million people which is 8.9% of the total population of the country. Patients were followed until 31st December 2015 to find vital status for survival analysis, using the patients' identification number from the Civil Registration Database maintained by the Thai Ministry of the Interior. Additional clinical information and treatment outcome information was obtained from Medical Record Liberian and Hospital Statistics, Faculty of Medicine, Chiang Mai University.

Data analysis

The incidence rates were calculated as mean annual numbers per 1,000,000 inhabitants for the period 1998-2012. Age-standardized incidence rates (ASRs) were calculated by the direct method of standardization by weighing age-specific incidence rates to the World Population (Doll et al., 1966; Parkin et al., 1988; Mirabello et al., 2009a). Population denominators to calculate incidence rates by sex, age group and province were estimated from the two population censuses surveyed in 1990, 2000 and 2010 (census, 1992; census, 2002; census, 2012). Osteosarcoma subtypes were classified following the International Classification of Diseases for Oncology (ICD-O-3 codes, 2000). Patient survival was calculated using Kaplan-Meier curve, median survival rate, and overall survival rate.

Results

Demographic data and geographic distribution

There were 148 newly diagnosed cases of osteosarcoma during 1998 to 2012. Of those, thirteen cases of head and neck and rib osteosarcoma plus one case of extraosseous osteosarcoma were excluded from this study leaving 144 cases for analysis. The average number of osteosarcomas occurring in northern Thailand during that period was 10 (±3) cases per year. The distribution of cases by province is shown in Figure 1A. In terms of anatomical location, the femur was the most common site (55.6%), followed by the tibia (16.8 %), pelvis (13%) and the humerus (5.2%) (Figure 1B). Conventional osteosarcoma was the most common cellular subtype (82%) (Figure 1C).

Age standardized incidence rate (ASR)

The median age at diagnosis was 17 years (range 4 to 80 years). The most frequent age group for osteosarcoma was 0 to 24 years (71.53%), while 23.61% were 25 to 59 years, and 4.86% were over 60 years. All osteosarcoma cases in patients age over 60 were recorded as primary osteosarcoma. The overall annual incidence of osteosarcoma was 1.67 per million with a male:female ratio of 1.36:1. Incidence by age group (0 to 24, 25 to 59 and over 60 years) and by gender (male and

female) were 3.5 (3.9 and 3.0), 0.8 (0.9 and 0.6), 0.7 (0.8 and 0.5), respectively. The male : female ratios for those age groups were 1.3:1, 1.5:1, and 1.6:1, respectively. An incidence peak occurred at 15 to 19 years for males (8.4 cases/million/year), and at 10 to 14 years for females (5.9 cases/million/year) (Figure 2A). The age-standardized incidence rates of osteosarcoma are shown in Figure 2B.

Survival rates of osteosarcoma

The median survival time was 18 months; the 5- and the 10-year overall osteosarcoma survival rates were 43% and 25%, respectively (Figure 2C). There was no significant difference in survival between the 0-24 age group and the >25 age group, p=0.139 (Figure 2D). Likewise, there was no significant difference in survival among the five-year periods of treatment, p=0.445 (Figure 2E).

Discussion

Determination of the incidence of osteosarcoma in specific geographic areas helps expand the epidemiological understanding of the relationship between genetic status and environmental exposure. Previous incidence reports from Thailand included only small geographic areas, analyzed only a young age group, or were non-population based analyses. Wiangnon et al. studied the incidence patterns of childhood cancer at 18 cancer centers, but only for patients 0 to 15 years of age. That study found an age-standardized rate incidence of osteosarcoma of 1.9 cases/million/year with a male:female ratio of 1.4:1. Wiromrat et al. reported the incidence of pediatric osteosarcoma in patients age 0-19 years in a single Thai province, Khon Khaen. In that study, the age-standardized incidence rate was 3.1 with a male:female ratio of 1:1 (Wiromrat et al., 2012). Mirabello et al. studied the international incidence of osteosarcoma. That study used the Chiang Mai province database registry for 1983 to 1997 to represent the incidence in Thailand (Mirabello et al., 2009a). The incidence reports from previous population-based studies in Thailand plus the present study are summarized in Table 1.

This paper is the first which systematically reviews osteosarcoma cases in Thailand in all age ranges. Data were collected from two cancer registry centers covering a large geographic area. We found a unimodal age distribution with the peak incidence occurring in the second decade of life. The findings are similar to age-standardized incidence rates reported from Europe (excluding UK), Asia and Latin America (Mirabello et al., 2009a). The peak age for females in this study (10-14 years) is younger than that of males (15-19 years), which is consistent with reports from other countries (Mirabello et al., 2009a; Mirabello et al., 2009b). Incidence rates in this study for the elderly group (0.8 and 0.5 per million for males and females, respectively) are lower than the average of Asian ethnic groups (3.1 and 2.4 in males and females, respectively), and much lower than those of the UK (5.4 and 3.4), USA (4.9 and 3.8), Canada (4.9 and 3.6) and Australia (7.0 and 3.5) (Mirabello et al., 2009b). High incidence of osteosarcoma in the elderly has been found to be closely related to a high incidence of Paget's disease in the Caucasians (Mirabello et al., 2009a; Corral-Gudino et al., 2013). Only 13 cases of Paget's disease have been report from Southeast Asia (Sirikulchayanonta et al., 2012). We found no Paget disease-related osteosarcoma in this study which is in line with a recent report on multicenter study of the Asian population which did not observe Paget's osteosarcoma in any of 232 osteosarcoma patients (Joo et al., 2015).

The median survival time and overall 5-year survival of Northern Thai osteosarcoma patients from previous analyses were 21.2 months and 37.9%, respectively (Pruksakorn et al., 2015). The result of treatment was relatively poor compared to other series. Factors associated with lower survival rates included advanced stage at initial diagnosis and poor compliance with treatment. The proportion of cases with advanced stage at initial evaluation (45.8%) was higher than other series (Pruksakorn et al., 2015). Lower proportion of initial metastasis cases were found in the USA by Mankin et al. (12%) (Mankin et al., 2004) and by Kaste et al. (15-20%) (Kaste et al., 1999), and found in the Cooperative Osteosarcoma Study Group Protocol (9.6%), by Bielack et al. (Bielack et al., 2002). Chemotherapeutic regimens which depend on two drugs were regularly used until the year 2012. Then high dose Methotrexate was added to the regimen for pediatric osteosarcoma (Choeyprasert et al., 2014). Long term survival analysis of this series will be conducted in the future.

In summary, this study is a large population-based incidence report of osteosarcoma in all age groups in northern Thailand. The average annual incidence was 1.67 cases/million with a male:female ratio of 1.36:1. No bimodal age distribution pattern was found. The trend of incidence and survival rates has not changed significantly over the last 15 years.

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