Inferior Clinical Outcomes of Pediatric Rhabdomyosarcoma in Thailand: A 16-Year Experience in a Single Tertiary Institution

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Abstract

Introduction: There is limited data available on the treatment outcomes of pediatric rhabdomyosarcoma (RMS) in Asian populations. Therefore, we aimed to review the baseline characteristics, clinical outcomes, and prognostic factors in children with RMS from Thailand. Methods: The data of children under 15 years of age diagnosed with RMS between 2003 and 2019 from a large tertiary hospital in Southern Thailand were retrospectively reviewed. Descriptive statistics were utilized to describe the clinical characteristics. The Kaplan–Meier method was utilized to estimate survival. Cox proportional hazards regression analysis was utilized to determine prognostic factors that affect survival. Results: A total of 42 children RMS were included in this study. The median age at diagnosis was 6.4 years (IQR, 2.4–10.2). Among these patients, 11 (26%) were older than 10 years, and 13 (31%) presented with metastatic disease at diagnosis. The 5-year overall survival (OS) rate was 39% for all children. Age greater than 10 years (hazard ratio (HR): 3.3, 95% CI: 1.2–9.2) and metastatic disease at diagnosis (hazard ratio (HR): 2.8, 95% CI: 1.1–7.5) were independently associated with poorer survival. The 3-year OS for children with metastatic disease (stage IV) was 15% (95% CI: 4.3–55). Conclusion: The percentage of metastatic disease in our cohort was higher than that in previous reports and may have contributed to a poorer outcome. Age greater than 10 years and metastatic disease at diagnosis were noted as adverse prognostic factors.

Keywords: Childhood cancer- rhabdomyosarcoma- survival outcome- prognostic factors- Asians

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Rhabdomyosarcoma (RMS) is the most prevalent soft tissue sarcoma, accounting for 3% of all pediatric cancers (Meyer and Spunt, 2004; Amer et al., 2019). The age-standardized incidence rate (ASR) is 4.4 per million children (Perez et al., 2011). In Asian countries, the incidence of RMS is less frequent than that in western countries, with the ASR ranging from 1.8–3.0 per million children (Wiangnon et al., 2011; Liu et al., 2015). The reported prognostic factors associated with survival include: age at diagnosis, pre-treatment TNM staging, primary site, histology subtype, and operable status (Dasgupta et al., 2016). In Western studies, the 5-year overall survival (OS) for RMS ranges from 30 to 90% (Meza et al., 2006; Amer et al., 2019). In Asian countries, the survival outcome varies from 10 to 80% (Bhurgri et al., 2004; Salman et al., 2012).

While 80% of childhood cancer patients reside in low-and middle-income countries (LMIC), there is limited data available on the treatment outcomes reported from Southeast Asian countries (Rodriguez-Galindo et al., 2015). Disparities in cancer treatment among LMIC and western countries have existed for decades (Bhatia, 2011). In Thailand, a previous population-based registry analysis showed that the 5-year OS for children with RMS ranged from 28 to 50%, which was much lower than the reported outcome from an international study (Wiangnon et al., 2011; Wiangnon et al., 2014; Bidwell et al., 2019).

Our study aimed to describe the baseline characteristics and clinical outcomes as well as to determine the prognostic factors of children diagnosed with RMS at the Songklanagarind hospital in Thailand, a middle-income country, and to compare these results with those from other Asian countries.

Materials and Methods

We retrospectively reviewed the medical documents of all children aged under 15 years who were diagnosed...
with RMS at Songklanagarind hospital, the biggest tertiary hospital in Southern Thailand, between November 2003 and September 2019. The diagnosis of RMS was confirmed based on the pathological report. The data collected included demographics, clinical characteristics, histology, staging, clinical group, risk group classification, and treatment outcomes. The pre-treatment staging of RMS was defined as stage I-IV based on primary site, tumor size, regional node involvement, and metastatic disease (TNM staging) (Lawrence et al., 1997). The clinical group classification was defined as group I–IV, contingent on the magnitude of residual disease after surgery. In brief, group I–II included children who postoperatively achieved grossly total resection of tumor (GTR). Group III included children with localized grossly residual tumor, and group IV represented those with distant metastasis at diagnosis (Sangkhathat, 2015; Rhee et al., 2020). Risk stratification into low risk, intermediate risk, and high risk, was based on pre-treatment TNM staging system, histology, and clinical group as described by the International Rhabdomyosarcoma Study Group (IRSG) (Hayes-Jordan and Andrassy, 2009; Malempati and Hawkins, 2012). The treatment plan was dependent on the period of diagnosis. Prior to 2015, all children in our cohort received the standard VAC regimen comprising of vincristine, actinomycin-D and cyclophosphamide 2.2 g/m²/cycle, based on IRSG-IV study (Crist et al., 2001; Arndt et al., 2009). In 2015, the Thai Pediatric Oncology Group (Thai-POG) proposed a national protocol defined by prognostic risk group stratification, in which low-risk patients received VAC (with cyclophosphamide 1.2 g/m²/cycle) for four cycles followed by VA for four cycles (Walterhouse et al., 2014), while intermediate-risk patients received the standard VAC regimen. The Thai-POG protocol for high-risk patients comprised an alternating intensive 6-drug combination, including ifosfamide, vincristine, etoposide, carboplatin, actinomycin-D, and cyclophosphamide (IVA/ChE/IVE/VAC) (Thai Pediatric Oncology Group, 2014).

**Statistical analysis**

Descriptive statistics were utilized to present clinical characteristics. For continuous variables, median and interquartile range (IQR) were used, and for categorical variables, frequency with percentage. The overall survival curve was depicted by the Kaplan–Meier method. Prognostic factors associated with clinical outcomes were evaluated using the Cox proportional hazards model in univariate and multivariate analysis. From the univariate analysis, prognostic factors having a p value less than 0.2 were included in the multivariate logistic regression model for the assessment of independent prognostic factors. Statistical significance was defined as a p value of less than 0.05. All analyses were performed in R program version 4.1.0 (The R Foundation for Statistical Computing, Vienna, Austria).

**Results**

There were 45 children diagnosed with RMS during the 16-year study period. We excluded three children who had incomplete data; two children had received treatment at other centers; one child presented with advanced stage disease and eventually died prior to treatment. A total of 42 children were included in the analysis with a median follow-up time of 23.6 months (range, 11.6 – 60.9). Demographic data, clinical characteristics and clinical outcomes are presented in Table 1. The median age at diagnosis was 6.4 years (IQR 2.4–10.2). Of the 42 children, 31 (74%) were younger than 10 years of age. The male to female ratio was 2.3:1. Embryonal RMS was the most frequent histologic subtype (40%). The primary tumor site was unfavorable in 33 (79%) children. The tumor size at diagnosis was larger than 5 cm in 29 (69%) children. Fourteen (33%) children had regional lymph node involvement at diagnosis, and 13 (31%) presented with metastatic disease at diagnosis. The distant metastatic sites included lungs (n=9), bone (n=6), bone marrow (n=2), and brain (n=1). Of these, six patients had two concurrent metastatic sites. All children with metastatic disease had a tumor size larger than 5 cm. The TNM pre-treatment staging were stage I, II, III, and

**Table 1. Clinical Characteristics and Outcomes of 42 Children with Rhabdomyosarcoma**

| Characteristics                  | n  | (%) | 5-year OS (95% CI) | P value |
|----------------------------------|----|-----|-------------------|---------|
| Median age at diagnosis (years)  | 6.4| (2.4–10.2) | 51 (36–72) | 0.011 |
| Age <10 years                    | 31 | (74%) | 51 (36–72) | 0.011 |
| Age ≥10 years                    | 11 | (26%) | -- (-- --) | 0.9   |
| **Sex**                          |    |     |                   |         |
| Male                             | 29 | (69%) | 38 (23–62) | 0.9   |
| Female                           | 13 | (31%) | 46 (26–83) | 0.9   |
| **Histology**                    |    |     |                   |         |
| Embryonal                       | 17 | (40%) | 39 (21–73) | 0.9   |
| Alveolar                         | 11 | (26%) | 32 (13–80) | 0.9   |
| Undetermined                     | 14 | (34%) | 42 (22–79) | 0.9   |
| **Primary tumor site**           |    |     |                   |         |
| Favorable                        | 9  | (21%) | 52 (27–100) | 0.3   |
| Unfavorable                      | 33 | (79%) | 37 (23–59) | 0.3   |
| **Tumor size (cm)**              |    |     |                   |         |
| ≤5                               | 13 | (31%) | 60 (38–95) | 0.069 |
| >5                               | 29 | (69%) | 31 (17–56) | 0.5   |
| **Regional nodes**               |    |     |                   |         |
| N0                               | 28 | (67%) | 37 (22–61) | 0.5   |
| N1                               | 14 | (33%) | 48 (27–85) | 0.5   |
| **Extent of disease**            |    |     |                   |         |
| Localized                        | 29 | (69%) | 53 (37–76) | 0.007 |
| Distant metastasis               | 13 | (31%) | -- (-- --) | 0.007 |
| **Post-operative group**         |    |     |                   |         |
| I–II                             | 12 | (29%) | 71 (48–100) | 0.006 |
| III                              | 17 | (40%) | 40 (22–72) | 0.006 |
| IV                               | 13 | (31%) | -- (-- --) | 0.001 |
| **Prognostic risk group**        |    |     |                   |         |
| Low risk                         | 13 | (31%) | 83 (64–100) | 0.001 |
| Intermediate risk                | 16 | (38%) | 29 (13–64) | 0.001 |
| High risk                        | 13 | (31%) | -- (-- --) | 0.001 |

IQR, interquartile range; OS, overall survival rate.
IV in 8 (19%), 4 (10%), 17 (40%), and 13 (31%) children, respectively.

The post-operative clinical group were evaluated after surgery; 12 (29%) were classified as post-operative group I–II (achieved GTR) 17 (40%) as group III, and 13 (31%) as group IV. According to prognostic risk group stratification, 13 (31%) were determined as low risk, 16 (38%) as intermediate risk and 13 (31%) as high risk. All children in our cohort received chemotherapy; 36 (86%) children received standard VAC regimen. Four children in the high-risk group received the IV A/CbE/IVE/V AC regimen, whereas two children in the low-risk group received VAC for four cycles and additional VA for four cycles. Thirty-eight (90%) children received radiotherapy.

The 5-year OS and EFS rates for all children with RMS were 39% (95% CI; 27–58) and 38% (95% CI; 26–56), respectively. The 5-year OS for children less than 10 years of age was 51% (95% CI; 36–72) vs 0% for those more than 10 years of age, p value = 0.011. The median survival time for the latter was 14.8 months (range, 1.5–56.4). Thirteen children with metastatic disease showed a dismal outcome with 3-year OS rate of 15% (95% CI; 4.3–55). Of these, 11 children eventually died from disease progression.

Children in clinical groups I–II, wherein the tumor could be totally resected, had better survival outcomes than those who underwent only biopsy or incomplete resection (clinical group III), with a 5-year OS rate of 15% (95% CI; 4.3–55). Of these, 11 children eventually died from disease progression.

Table 2. Univariate Analysis of Prognostic Factors Associated with RMS Outcomes

| Prognostic factors                  | Overall survival | Hazard ratio | P value |
|------------------------------------|------------------|--------------|---------|
| Age at diagnosis                   |                  |              |         |
| <10 years                          | Ref              | 0.015        |         |
| ≥10 years                          | 2.9 (1.2–6.8)    |              |         |
| Tumor size                         |                  |              |         |
| ≤5 cm                              | Ref              | 0.078        |         |
| >5 cm                              | 2.4 (0.9–6.5)    |              |         |
| Regional node involvement          |                  |              |         |
| Negative                           | Ref              | 0.46         |         |
| Positive                           | 0.7 (0.3–1.7)    |              |         |
| Extent of disease                  |                  |              |         |
| Localized                          | Ref              | 0.01         |         |
| Distant metastasis                 | 3.0 (1.3–7.0)    |              |         |
| Gross total resection              |                  |              |         |
| Post-operative clinical group I–II | Ref              | 0.015        |         |
| Post-operative clinical group III–IV| 4.6 (1.4–15.0)  |              |         |
| Radiotherapy                       |                  |              |         |
| Yes                                | Ref              | 0.037        |         |
| No                                 | 3.8 (1.1–13.4)   |              |         |
| Prognostic risk group              |                  |              |         |
| Low                                | Ref              | 0.008        |         |
| Intermediate                       | 7.3 (1.6–33.0)   |              |         |
| High                               | 11.0 (2.5–53.0)  |              |         |

Ref, reference; RMS, rhabdomyosarcoma

Table 3. Multivariate Analysis of Prognostic Factors Associated with RMS Outcomes

| Prognostic factors                  | Overall survival | Hazard ratio | P value |
|------------------------------------|------------------|--------------|---------|
| Age at diagnosis                   |                  |              |         |
| <10 years                          | Ref              | 0.021        |         |
| ≥10 years                          | 3.3 (1.2–9.2)    |              |         |
| Tumor size                         |                  |              |         |
| ≤5 cm                              | Ref              | 0.508        |         |
| >5 cm                              | 1.5 (0.4–4.9)    |              |         |
| Extent of disease                  |                  |              |         |
| Localized                          | Ref              | 0.032        |         |
| Distant metastasis                 | 2.8 (1.1–7.5)    |              |         |

Ref, reference; RMS, rhabdomyosarcoma
to their prognostic risk group. The 5-year OS of children in the low-risk group was 83% while that of children in the intermediate risk group was 29% (p value < 0.001). (Figure 2)

The 5-year EFS for children diagnosed before 2015 (n = 30) was 29% compared to 64% in those diagnosed after 2015 (n = 12) (p value = 0.035). The percentage of metastatic disease was not different between the two eras, but children who received treatment after 2015 seemed to have a higher rate of surgical management (75% vs. 60%, p value = 0.485) although not statistically significant.

In univariate analysis, five prognostic factors that were statistically associated with overall survival outcome included: age greater than 10 years, presence of metastatic disease at diagnosis, gross total resection, radiotherapy, and prognostic risk group, as shown in Table 2. Children who failed to achieve GTR (HR 4.6, 95% CI: 1.4–15.0) or had metastatic disease (HR 3.0, 95% CI: 1.3–7.0) were correlated with worsened outcomes. Children who had not received radiotherapy also had lower OS rates (HR 3.8, 95% CI: 1.1–13.4) while chemotherapy regimen did not affect the survival in our study. Prognostic risk

| Country      | First Author /Year | N     | Study period     | Metastasis at diagnosis (%) | 5-year OS | 5-year OS (%) by prognostic risk group |
|--------------|--------------------|-------|------------------|-----------------------------|-----------|---------------------------------------|
| China        | Ma 2015            | 161   | 2001–2014        | 37.3                        | 65.3†     | 100† Low risk                          |
|              | Xu 2019            | 213   | 2006–2018        | 25.8                        | 64        | 100 Intermdiate risk                   |
| Hongkong     | Yuan 2008          | 19    | 1989–2005        | 31.6                        | 42        | 66 High risk                           |
| Iran         | Company 2011       | 60    | 1996–2002        | 40                          | 47.9      | 71 Low risk (IRS-II)                   |
|              | Bansal 2017        | 77    | 1990–2012        | 11                          | 43.6†     | NA Intermediate risk                   |
| Swaminathan  | 2008               | 42    | 1990–2001        | NA                          | 36.4      | NA High risk                           |
| Japan        | Hosoi 2007         | 331   | 1991–2002        | 23.2                        | 60.7      | 94 Low risk (IRS-II)                   |
| Korea        | Park 2008          | 77    | 1986–2005        | 24.7                        | 77        | 100 Low risk (IRS-I-II)                |
|              | Lee 2018           | 51    | 2001–2015        | 45.1                        | 63.8      | ERMS 5-year OS = 75.1% ARMS 5-year OS = 33.6% |
| Lebanon      | Salman 2012        | 23    | 2002–2010        | 4.4                         | 83        | NA                                     |
| Pakistan     | Bhurgi 2004        | 100   | 1998–2002        | NA                          | 10        | NA                                     |
| Singapore    | Aung 2014          | 50    | 1993–2010        | 24                          | 80.3      | 81.3‡ Intermediate risk                |
| Taiwan       | Chou 2019          | 37    | 1995–2016        | 32.4                        | 54.7      | 83.3 High risk                         |
| Turkey       | Akyüz 2012         | 409   | 1973–2003        | 11                          | 34        | 50-71 Low risk (IRS-II)                |
|              | Sezgin 2015        | 24    | 2000–2011        | NA                          | 40.1-68.2 | NA                                     |
| Thailand     | Wiangnon 2011      | 178   | 1990–2011        | NA                          | 28.5      | NA                                     |
|              | Bidwell 2019       | 137   | 2003–2005        | NA                          | 50.1      | NA                                     |
| IRS-IV study | Crist 2001, Raney 2001 | 883 | 1991–1997 | 16 | 71 | 80-99 High risk                          |
| Current study |                  | 42    | 2003–2019        | 30.9                        | 39        | 83 High risk (IRS-IV)                  |

Abbreviations: ARMS, alveolar rhabdomyosarcoma; ERMS, embryonal rhabdomyosarcoma; IRS, International Rhabdomyosarcoma Study; LR, low risk; IR, Intermediate risk; HR, high risk; NA, data not available; OS, overall survival rate; † Data are presented as the 10-year overall survival rate; ‡ Data are presented as the 5-year event-free survival rate.

Figure 2. The Overall Survival of Children with RMS, According to Prognostic Risk Stratification
group was strongly associated with the survival outcome (p value = 0.008).

In multivariate analysis, the independent prognostic factors associated with end outcome are shown in Table 3. The two prognostic factors associated with a poor outcome were age greater than 10 years (HR: 3.3, 95% CI: 1.2–9.2) and metastatic disease at diagnosis (HR: 2.8, 95% CI: 1.1–7.5).

Discussion

Our study was a descriptive analysis of clinical characteristics, survival outcome, and adverse prognostic factors in children with RMS from Southern Thailand. The majority of our children (74%) were aged below 10 years, similar to those in international studies (Perež et al., 2011; Weiss et al., 2013; Amer et al., 2019). In our study, the 5-year OS rate of children with RMS was 39% (95% CI: 27–58). In western countries, data from IRS-IV studies reported a 5-year OS rate of 71% (Crist et al., 2001). Overall, the 5-year OS rate for children with RMS in Asian countries was lower than that in children in studies from western countries, except those from Lebanon and Singapore, where the 5-year OS rate was comparable to that of western studies (Salmon et al., 2012; Aung et al., 2014). In Thailand, previous reports on RMS were solely from population-based studies focusing on the incidence and crude survival rate of childhood cancer (Wiangnon et al., 2011; Wiangnon et al., 2014; Bidwell et al., 2019).

Despite the rarity of the disease, RMS usually appears insidiously among children. In our study, 31% of the affected children (n=13) showed distant metastasis at diagnosis, which is twice times higher than the rates from western studies (16%) (Weiss et al., 2013). This might be explained by the fact that our hospital is the only university hospital and one of two pediatric cancer referral centers in Southern Thailand. Therefore, most patients in our cohort visited the local municipality for investigation and were further referred to us for diagnosis and treatment. Badr (2012) found that 44% of children with RMS in Egypt presented with metastatic disease at diagnosis, which mainly was explained by lack of recognition of presenting symptoms by the primary health care providers and unavailability of facilities for early diagnosis (Abd El-Aal et al., 2006). This finding was similar to previous reports from China, Hongkong, Iran, Japan, Korea, Taiwan, and Singapore, wherein metastasis on diagnosis ranged from 23–45% as shown in Table 4 (Hosoi et al., 2007; Park et al., 2008; Yuan et al., 2008; Company et al., 2011; Ma et al., 2015; Lee et al., 2018; Xu et al., 2019). In South Asia, South East Asia or the Middle East, descriptive data regarding of clinical characteristics of childhood RMS and its local outcomes were scarce (Wiangnon et al., 2011; Bansal et al., 2017; Bidwell et al., 2019).

About 69% of children in our cohort had tumors larger than 5 cm. The median time from symptom presentation to diagnosis was 8 weeks (range, 4–28). Therefore, the delayed diagnosis from the lack of awareness of parents and primary care physicians about early signs of cancer was the contributing factor to the higher metastatic disease in this study. The advanced stage of disease was attributed to the inferior outcomes. Thus, education for general practitioners and public awareness raising are needed to build the expertise for early cancer diagnosis. The comprehensive referral network might also shorten the duration of diagnosis and investigation.

In our cohort, the histology subtype was not associated with final outcome while previous reports showed a strong correlation between histology subtype and pattern of distant metastasis on end outcome (Meza et al., 2006; Weiss et al., 2013). This might be explained by the limited sample size and retrospective nature of our study, wherein the histologic subtype was undetermined in 32% of the affected children.

The outcome of RMS appears dependent on many factors, which formed the prognostic risk group (Malempati and Hawkins, 2012). From the IRS-III-IV study, the 5-year OS rates were 95–98% for low risk, 59–83% for intermediate-risk and 30% for high-risk RMS (Raney et al., 2001)(Table 4). In our cohort, the 5-year OS of children in the low risk group was 83%, which was comparable to the that in the IRS study and our neighboring countries, like Singapore (5-year EFS 81.3%) (Aung et al., 2014) or Taiwan (Chou et al., 2019). However, the survival for children in the intermediate risk group was much lower than that reported in other Asian countries and the IRS study. The 5-year OS rate for this group was 29%, in contrast to 59–83% from the IRS studies (Crist et al., 2001; Raney et al., 2001). This finding might be explained by a low GTR rate (28%) in our cohort and even lower in the intermediate risk group (19%).

Our study identified two adverse prognostic factors from the multivariate analysis using the Cox regression model to predict inferior overall survival, including age older than 10 years and the presence of distant metastases at diagnosis. This finding conformed to previous studies; Joshi (2004) reported that the 5-year EFS for children aged 1–9 years (72%) was significantly better than that in infants (53%) and children age above 10 years old (51%) (p < 0.001). The particularly poor outcome for children older than 10 years old in our cohort was mainly explained by the advanced stage at diagnosis. In this group, 4 of 11 children (36%) presented with metastatic disease at diagnosis and 10 of 11 children (91%) had tumor sizes larger than 5 cm at diagnosis. Total resection was achievable in only 3 of 11 children (27%) in this group, which then resulted in a poor outcome. This finding concorded with the previous report by Badr (2012), which found that the 5-year OS for children aged > 10 years was only 25%.

The 3-year OS for metastatic RMS in our study was 15%, which lower than previous report from Bailey (2020) that stated a 3-year OS for metastatic RMS of 34% and that those with bone marrow metastasis showed the worst prognosis, with a 3-year OS of 14% (Rudzinski et al., 2017). Oberlin (2008) reported a strong correlation of four adverse factors and worse prognosis: age above 10 years, unfavorable primary tumor site, bone or bone marrow involvement, and presence of three or more metastatic sites. All children who had metastatic disease in our cohort were aged above 10 years; 93% had unfavorable primary site tumor, and two children had an Oberlin score of 3.
In our cohort, the treatment outcome improved over time from a 5-year EFS at 29% in the earlier period to 64% in the later five years. The improvement of treatment outcomes during the last 5 years (2015–2020) was mainly explained by the increasing trend of surgical management. This was in concordance with the result of the IRS-G studies wherein the 5-year OS rate continuously improved from 55% in IRS-I study to approximately 71% in the IRS-III and IRS-IV studies (Raney et al., 2001).

Our study had some limitations. First, the retrospective design of this study might be associated with potential bias. Further, some clinical characteristics such as histologic subtype were unavailable. Second, the small sample size was insufficient for comparison between different chemotherapy protocols. Lastly, genetic abnormalities or PAX-FOXO1 fusion status, which strongly adversely affects outcome and had been recently included in risk stratification, was not screened in this study (Rudzinski et al., 2017; Hibbitts et al., 2019; Heske et al., 2021).

In conclusion, survival outcomes for pediatric RMS from one institution in Thailand were inferior to those in developed countries but were comparable to those in other developing countries in Asia. After stratification according prognostic risk group, children in the low-risk group showed outcomes comparable to those in international studies; however, the survival outcome in both intermediate and high-risk groups were far below those from international studies. A high percentage of metastatic disease at diagnosis in developing countries may adversely influence the outcome. This reflects a need for effective strategies, such as early diagnosis, increased attempts for GTR, and comprehensive multidisciplinary care, to enhance the clinical outcome for children with RMS in developing countries.

Author Contribution Statement

All authors contributed significantly to both the research and the composition of the work, and they all reviewed and approved the final version.

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Ethics statement

This study was granted ethical approval by the Ethics Committee of the Faculty of Medicine, Prince of Songkla University, Songkhla, Thailand.

Data availability statement

The data supporting the study results is obtainable upon request from the corresponding author. Due to privacy and ethical concerns, the data is not publicly accessible.

Conflict of Interest

The authors declare that they have no conflict of interest.

References

Abd El-Aal HH, Habib EE, Mishrif MM (2006). Rhabdomyosarcoma: the experience of the pediatric unit of Kasr El-Aini Center of Radiation Oncology and Nuclear Medicine (NEMROCK) (from January 1992 to January 2001). J Egypt Nail Cancer Inst, 18, 51–60.

Akyüz C, Sari N, Yalçin B, et al (2012). Long-term survival results of pediatric rhabdomyosarcoma patients: a single-center experience from Turkey. Pediatr Hematol Oncol, 29, 38-49.

Amer KM, Thomson JE, Congiusta D, et al (2019). Epidemiology, Incidence, and Survival of Rhabdomyosarcoma Subtypes: SEER and ICES Database Analysis. J Orthop Res Off Publ Orthop Res Soc, 37, 2226–30.

Arndt CAS, Stoner JA, Hawkins DS, et al (2009) Vincristine, actinomycin, and cyclophosphamide compared with vincristine, actinomycin, and cyclophosphamide alternating with vincristine, topotecan, and cyclophosphamide for intermediate-risk rhabdomyosarcoma: children’s oncology group study D9803. J Clin Oncol, 27, 5188–26.

Aung L, Soe TA, Chang KT, Quah TC (2014). Singapore rhabdomyosarcoma (RMS) experience: shall we change our practice?: Ann Acad Med Singapore, 43, 86–95.

Badr MA, Al-Tonbary YA, Mansour AK, et al (2012). Epidemiological characteristics and survival studies of rhabdomyosarcoma in East Egypt: a five-year multicenter study. ISRN Oncol, 2012, 674523.

Bailey KA, Wexler LH (2020). Pediatric rhabdomyosarcoma with bone marrow metastasis. Pediatr Blood Cancer, 67, e28219.

Bansal D, Das A, Trehan A, et al (2017). Pediatric Rhabdomyosarcoma in India: A Single-center Experience. Indian Pediatr, 54, 735–8.

Bhatia S (2011). Disparities in cancer outcomes: lessons learned from children with cancer. Pediatr Blood Cancer, 56, 994–1002.

Bhurgri Y, Bhurgri A, Puri R, et al (2004). Rhabdomyosarcoma in India: A Single-center Experience. Pediatr Blood Cancer, 43, 54–60.

Bidwell SS, Peterson CC, Deman仕lis K, et al (2019). Childhood cancer incidence and survival in Thailand: A comprehensive population-based registry analysis, 1990-2011. Pediatr Blood Cancer, 66, e27428.

Chou S-W, Chang H-H, Lu M-Y, et al (2019). Clinical outcomes of pediatric patients with newly diagnosed rhabdomyosarcoma treated by two consecutive protocols - A single institution report in Taiwan. J Formos Med Assoc, 118, 332–40.

Company F, Pedram M, Rezaei N (2011). Clinical characteristics and the prognosis of childhood rhabdomyosarcoma in 60 patients treated at a single institute. Acta Med Iran, 49, 219–24.

Crist WM, Anderson JR, Meza JL, et al (2001). Intergroup rhabdomyosarcoma study-IV: results for patients with nonmetastatic disease. J Clin Oncol, 19, 3091-102.

Das Gupta R, Fuchs J, Rodeberg D (2016). Rhabdomyosarcoma. Semin Pediatr Surg, 25, 276-83.

Hayes-Jordan A, Andrassy R (2009). Rhabdomyosarcoma in children. Curr Opin Pediatr, 21, 373–8.
Heske CM, Chi Y-Y, Venkatramani R, et al (2021). Survival outcomes of patients with localized FOXO1 fusion-positive rhabdomyosarcoma treated on recent clinical trials: A report from the Soft Tissue Sarcoma Committee of the Children’s Oncology Group. Cancer, 127, 946–56.

Hibbitts E, Chi Y-Y, Hawkins DS, et al (2019). Refinement of risk stratification for childhood rhabdomyosarcoma using FOXO1 fusion status in addition to established clinical outcome predictors: A report from the Children’s Oncology Group. Cancer Med, 8, 6437–48.

Hosoi H, Teramukai S, Matsumoto Y, et al (2007). A review of 331 rhabdomyosarcoma cases in patients treated between 1991 and 2002 in Japan. Int J Clin Oncol, 12, 137–45.

Joshi D, Anderson JR, Paidas C, et al (2004). Age is an independent prognostic factor in rhabdomyosarcoma: a report from the Soft Tissue Sarcoma Committee of the Children’s Oncology Group. Pediatr Blood Cancer, 42, 64–73.

Lawrence W, Anderson JR, Gehan EA, Maurer H (1997). Pretreatment TNM staging of childhood rhabdomyosarcoma: a report of the Intergroup Rhabdomyosarcoma Study Group. Children’s Cancer Study Group. Pediatr Oncol Group Cancer, 80, 1165–70.

Lee DH, Park CJ, Jang S, et al (2018). Clinical and cytogenetic profiles of rhabdomyosarcoma with bone marrow involvement in Korean children: A 15-year single-institution experience. Ann Lab Med, 38, 132–8.

Liu Y-L, Lo W-C, Chiang C-J, et al (2015). Incidence of cancer in children aged 0–14 years in Taiwan, 1996-2010. Cancer Epidemiol, 39, 21–8.

Ma X, Huang D, Zhao W, et al (2015). Clinical characteristics and prognosis of childhood rhabdomyosarcoma: a ten-year retrospective multicenter study. Int J Clin Exp Med, 8, 17196–205.

Malempati S, Hawkins DS (2012). Rhabdomyosarcoma: review of the Children's Oncology Group (COG) Soft-Tissue Sarcoma Committee experience and rationale for current COG studies. Pediatr Blood Cancer, 59, 5–10.

Meyer WH, Spunt SL (2004). Soft tissue sarcomas of childhood. Cancer Treat Rev, 30, 269–80.

Meza JL, Anderson J, Pappo AS, et al (2006). Analysis of prognostic factors in patients with nonmetastatic rhabdomyosarcoma treated on intergroup rhabdomyosarcoma studies III and IV: the Children’s Oncology Group. J Clin Oncol, 24, 3844–51.

Oberlin O, Rey A, Lyden ER, et al (2013). Histologic and clinical characteristics can guide staging evaluations for children and adolescents with rhabdomyosarcoma: a report from the Children’s Oncology Group Soft Tissue Sarcoma Committee. J Clin Oncol, 31, 3226–32.

Wiangnon S, Jetsrisuparb A, Komvilaisak P, Suwanrugrug K (2014). Childhood cancer incidence and survival 1985-2009, Khon Kaen, Thailand. Asian Pac J Cancer Prev, 15, 7989–93.

Wiangnon S, Veerakul G, Nuchprayoon I, et al (2011). Childhood cancer incidence and survival 2003-2005, Thailand: study from the Thai Pediatric Oncology Group. Asian Pac J Cancer Prev, 12, 2215–20.

Xu N, Duan C, Jin M, et al (2019). Clinical and prognostic analysis of single-center multidisciplinary treatment for rhabdomyosarcoma in children. Zhonghua Er Ke Za Zhi, 57, 767–73.

Yuan XJ, Chan GCF, Chan SK, et al (2008). Treatment outcome of rhabdomyosarcoma with bone marrow involvement in Korean children: A 15-year single-institution study. J Pediatr Surg, 43, e243-51.

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