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Raising Awareness: Real World Data On Palliative Care for Advanced Pediatric Cancers in Bavaria

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ABSTRACT

Introduction: Early integration of palliative care in children with cancer provides a variety of positive effects and is recommended at diagnosis. However, barriers often delay its implementation, and palliative care remains underutilized. This study provides real-world data on palliative care and integration in pediatric oncology in a high-income country.

Methods: In this retrospective observational study, data derived from patients with refractory, progressive, or relapsed malignancies under the age of 18 years were collected from six German pediatric oncology centers (2017–2022). In addition to palliative data (onset, and duration of palliative care services, frequency of contact, place of death), disease entity, relapse/progression frequency, Karnofsky Performance Scale Index, therapy, and overall survival were collected. The frequency, timepoint of initiation and the duration of palliative care services were examined in relation to the disease trajectory (diagnosis to death/censoring) and tumor entity. Outcomes (overall survival, Karnofsky Performance Scale Index, place of death) were analyzed based on palliative care status.

Results: Only 157 (42%) of the 373 patients received palliative care services. The mean duration of palliative involvement was 6.0 months with a mean disease trajectory of 31.4 months for patients receiving palliative care. On average, palliative care was initiated in the last third of the disease trajectory. Most of the 157 patients (65.9%) received palliative care during their final relapse/progression and only 16.8% at diagnosis. There was a significantly lower frequency of palliative care involvement for children with hematological malignancies.

Abbreviations: ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; CNS, central nervous system; EOL, end-of-life; HRQOL, health-related quality of life; PPC, pediatric palliative care.

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Conclusion: Despite the substantial benefits, this study highlights significant delays and underutilization of palliative care for pediatric oncology patients, even in a high-income country.

1 | Introduction

Despite the steady rise in overall survival for children with cancer in recent decades [1], with 5-year survival rates of up to 80% in high-income countries [2], cancer remains the leading cause of disease-related death in children [3]. Additionally, patients suffer from multidimensional sequelae during their disease trajectory even after successful treatment, resulting in a poor overall health-related quality of life (HRQOL) [4, 5]. Pediatric palliative care (PPC) strives toward a holistic improvement in the well-being of pediatric cancer patients and is not limited to the patient, but also involves the extended family. Since the first WHO definition in 1998 [6], palliative care has become an integral part of oncology and its positive impact is extensive. Palliative care not only improves symptom burden and the HRQOL of patients and parents, but also leads to less intensive end-of-life (EOL) therapy and can have an impact on overall survival [7–12]. By definition, it is not limited to advanced stages of the disease and should be considered regardless of the therapeutic goal, even if it is curative [13]. Notably, an early integration of palliative care into oncological therapy demonstrated favorable effects and is now considered a standard of care [14]. Despite the proven substantial benefits, palliative care remains underused on a global scale. Limited resources are one of the main explanations, particularly in low-income countries [15]. However, the reasons are complex and can be attributed to structural factors, misconceptions, and socio-cultural aspects [16, 17]. While the current literature focuses on low- and middle-income countries, there are limited robust data on the current coverage and distribution of palliative care, beyond mono-institutional studies in high-income countries [18].

The aim of our study was to assess the current utilization of palliative care services in Bavaria in a subset of children with poor prognosis cancer through observational data, with a focus on distribution, initiation, and duration of such care. Furthermore, variables such as overall survival, Karnofsky Performance Scale Index, and place of death were analyzed based on whether children received palliative care services.

2 | Methods

2.1 | Study Design and Participants

The study was designed as a retrospective, nonexperimental observational study evaluating the status of palliative care for children with cancer in Bavaria. Data were acquired at six tertiary care centers in Bavaria, all of which are centers for pediatric oncology and members of the Pediatric Oncology Network Bavaria (Kinderonokologisches Netzwerk [in German]). All sites offer board-certified specialist in palliative care, who operate as part of an interdisciplinary palliative team. Each team included, at minimum, pediatricians and nurses with specialized training in palliative care, social workers, and chaplains. Patients under 18 years of age who presented with a relapse or refractory cancer at one of the centers between 2017 and 2022 were considered eligible for inclusion. Institutional ethics board approval was obtained at each site.

2.2 | Data Collection

The data were collected by each respective center from manual and electronic health records of the included patients. The patient data were anonymized by the respective center of care. Primary variables collected were: Involvement of the palliative team (yes/no), start of palliative care, duration of palliative care (months), and trajectory of disease (diagnosis to death/censoring in months). Secondary variables collected were: Karnofsky performance scale index (0–100), overall survival (diagnosis—death). Additional variables included were: mean contact frequency of the palliative team per month, location of death (hospital/hospice/home), tumor entity, age at diagnosis, number of relapses and number of tumor progressions, therapies received, and site of care.

2.3 | Data Analysis

Palliative, clinical, and demographic characteristics were summarized by descriptive statistics. Rate of palliative care was calculated for each diagnostic category (central nervous system [CNS] tumors, hematological malignancies: acute lymphoblastic leukemia [ALL], acute myeloid leukemia [AML], lymphoma, and solid malignancies: osseous sarcoma, soft-tissue sarcoma, neuroblastoma, nephroblastoma, others). Differences in the proportion of palliative care involvement based on tumor type was assessed using two tailed Fisher's exact test. We examined the initiation of palliative care in relation to the disease trajectory, by calculating the ratio of time from palliative care initiation to death/censoring relative to total disease trajectory. This ratio was expressed as a fraction of the total disease trajectory, where 0.00 indicates palliative care started at diagnosis, and higher values represent later initiation during the disease trajectory. For example, a ratio of 0.50 would indicate palliative care began halfway through the disease trajectory. In addition, the initiation of palliative care was evaluated in relation to the number of relapses. *T*-test was used to compare the age and Karnofsky performance scale index based on palliative care status. Survival analysis was done using Log-rank test. Relapse count with respect to the disease duration was evaluated using a negative binomial model, gender, and place of death were tested using Chi-squared tests. A two-sided significance level of $p < 0.05$ was chosen for each test and all statistical analysis was done in Python (Version 3.7) and R (Version 4.1).

TABLE 1 | Descriptive statistics based on palliative care status. Statistical tests showed significant differences in overall survival and place of death between both groups. Asterisks (*) indicate *p* values that meet the significance threshold as defined in the *Methods* section. “N/A” denotes that data were not available.

	Palliative care ($n = 157$)	No palliative care ($n = 216$)	*p* value
Age	7.8 ± 5.3 years	7.3 ± 5.2 years	0.36
Gender	M:87 F:70	M:138 F:78	0.09
	Entity		
CNS tumors	70 (44,6%)	77 (35.6%)	
Hematological malignancies	22 (14.0%)	66 (30.6 %)	
Solid tumors	65 (41.4%)	73 (33.8%)	
	Number of relapses		
Mean ± std	2.13 ± 1.3	1.68 ± 1.1	0.12
	Survival		<0.001*
Mean + std	37.1 ± 36.7 months	62.4 ± 41.9 months	
Died	128	30	
Alive/lost to follow-up	29	186	
	Place of death		<0.001*
Hospital	42 (32.8%)	14 (46.7%)	
At home	67 (52.3%)	5 (16.7%)	
Hospice	1 (0.8%)	0	
N/A	18 (14.1%)	11 (36.6%)	

3 | Results

3.1 | Patient Characteristics

In total, 373 patients with refractory or relapsed cancer were included. A total of 42% ($n = 157$) received palliative care of any kind (Table 1). The mean duration of palliative care involvement was 6.0 ± 6.9 months, while the mean disease trajectory of patients receiving palliative care was 31.4 ± 23.5 months. The average contact with the palliative care team per month was 5.6 ± 8.1 when reported, that is, every 6 days there was a contact between the palliative care team and the patient/parent. In the group of 157 patients who received palliative care at any time during our observation period, 81.5% ($n = 128$) children died within that period, compared with 13.9% ($n = 30$) in the group that did not receive palliative care. Significant differences were shown for overall survival (palliative care: 37.1 ± 36.7 months vs. no palliative care: 62.4 ± 41.9 months; $p < 0.001$). A negative binomial regression model was used to examine the influence of the number of relapses on palliative care services, adjusting for disease duration. The regression model revealed a significant association between the number of relapses and palliative care services ($\beta = 0.154$, standard error = 0.03, $p < 0.001$), indicating that a higher number of relapses is associated with increased utilization of palliative care services. No significant differences in the distribution of gender and age were observed based on whether patients received palliative care or not. Of the 81 patients with available end-of-life data who received palliative care, for 65.9% care began after diagnosis of the last relapse or progression. Only 16.8% received palliative care before the diagnosis of a cancer relapse or progression. For the remaining 17.3%, palliative care began between the diagnosis of the first and last relapse/progress. The disease trajectory of individual patients compared with the duration of palliative care services is visualized in Figure 1. In relation to the duration of the disease, median initiation of palliative care occurred after 83% (IQR 61%; 92%) of the total disease duration (Figure 2).

3.2 | Palliative Care by Tumor Type

The rate of palliative care involvement depending on the tumor type was as follows: CNS tumors = 47.6% ($n = 70/147$), hematological malignancies = 25.0% ($n = 22/88$), and solid tumors = 47.1% ($n = 65/138$). Using the CNS rate as a basis, due to the highest number of cases, a significantly lower rate for the hematological malignancies was found $p = 0.0006$ (OR CI95: 1.53; 4.93), while no significant differences were observed for solid tumors ($p = 1.000$; OR CI95: 0.84; 1.29). Hematological malignancies were divided into 55 cases of ALL, 22 cases of AML, and 11 cases of lymphoma.

3.3 | Impact of Palliative Care Services

In patients who did not receive palliative care, chemotherapy was administered less than 2 months prior to death in 25% of cases;

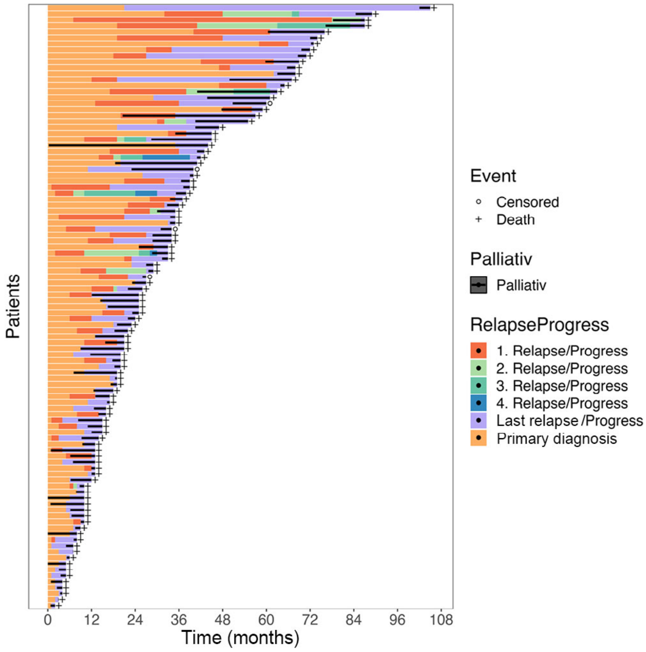

FIGURE 1 | Swimmer plot visualizing palliative care duration relative to disease progression and recurrence. The *X*-axis shows time in months, while color-coded bars on the *Y*-axis represent individual patients' disease duration and recurrence rate. Purple marks the last recurrence, and black shows palliative care duration.

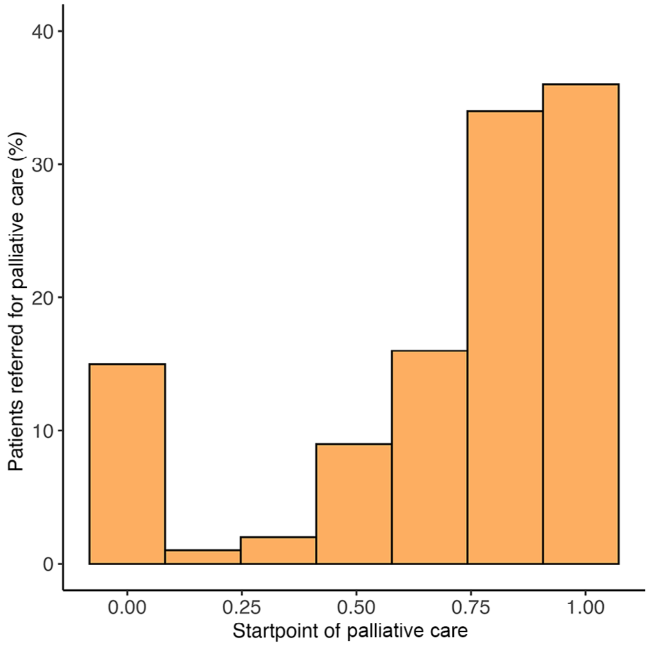

FIGURE 2 | Palliative care in relation to time of disease trajectory. The *Y*-axis shows patient frequency, and the *X*-axis represents the timing of palliative care during the disease. A value of 0 indicates onset at diagnosis. Palliative care most frequently begins in the last quarter of the disease trajectory.

if palliative care was provided at any time point, the percentage was 16.6% ($p = 0.41$). Of all patients receiving palliative care, 32.8% ($n = 42$) died in hospital, 52.3% ($n = 67$) died at home, 0.8% ($n = 1$) died in a hospice and for 14.1% ($n = 18$) no data were available. In contrast, patients who did not receive palliative care, showed a significantly different distribution, 46.7% ($n = 14$) died in hospital and 16.6 % ($n = 5$) died at home. No data were available for 36.7% ($n = 11$). When dichotomizing the place of death into hospital and non-hospital settings, patients who did not receive palliative care had a significantly higher rate of in-hospital death ($p < 0.001$).

4 | Discussion

Our observational study analyzes the palliative care situation for pediatric patients with advanced cancer in the six pediatric cancer centers in Bavaria. Of the 373 patients included, only 42% received palliative care services.

This low referral rate stands in stark contrast with the European and American guidelines [13, 19], which stipulate that palliative care should be made available to all children with a life-limiting or life-threatening condition, a definition that relapsing cancers clearly fulfill.

Germany ranks among the 10% of countries with the highest integration of palliative care into mainstream healthcare services [20], yet our observed referral rate of 42 % closely parallels what was reported in England between 1990 and 2005 [21], a country with a comparable integration of palliative care. Similarly, Davis et al. [22] found a referral rate for palliative care services of 58% in pediatric cancer cases in a primary referral center in the United States. These results indicate stagnation and stands in contrast to individual studies that have reported a marked increase in referral rates over the past decades [23].

As already shown for adult patients, palliative care involvement is less frequent for hematologic malignancies than for other malignancies [24]. Our analysis showed a significantly lower referral rate for palliative care services in hematological malignancies which is not limited to EOL therapy [25, 26]. The reasons for the difference remain unclear and warrant further investigation. A potential explanation may be the variability in disease course and the resulting prognostic uncertainty [27, 28]. Especially in pediatric patients, where the parents play a central role [29], uncertainty in the decision-making process may be further amplified.

In our cohort palliative care involvement in over 50% of cases was initiated in the last third of the disease trajectory, and in 65.9% no palliative care took place until the last relapse/progression. This is in line with the mono-institutional study by Johnston and Vadeboncoeur [30], which showed comparable referral rates for patients with advanced cancer despite the clear rationale for early initiation of palliative care. Patients in our study who received palliative care had lower rates of inpatient deaths, underscoring the potential benefits of early palliative care initiation.

Our findings, namely, the timing of referrals occurring primarily in the final stages of disease, the markedly shorter survival in the palliative care group, and the underutilization in hematological malignancies, demonstrate that palliative care remains predominantly associated with end-of-life care even in pediatric cancer centers in high-income countries such as ours. The marked difference in survival most likely reflects that patients with more aggressive disease trajectories and poorer prognoses are more likely to be referred. Consequently, referrals appear to be triggered by clinical deterioration rather than being integrated as a standard component of comprehensive cancer care highlighting the need for strategies and programs to promote earlier integration of palliative services in pediatric oncology. In addition to appropriate incentives, the implementation of guidelines for PPC involvement is essential to establish standardized care. A German guideline is scheduled for 2025 by relevant organizations.

Our study has several limitations, which are primarily determined by the retrospective study design. Using existing records without standardized quality control may result in missing or inconsistent data. Additionally, unmeasured confounders not captured in the records may have influenced our results. However, real-world data give a realistic view of the current care situation, which is the clear goal of our work. Furthermore, we were able to evaluate data from the leading cancer centers in Bavaria, ensuring that the results are not influenced by mono-institutional approaches.

Our results give a realistic representation of the palliative care situation in Bavaria, which, contrary to current recommendations, has clear deficits in the referral rate and in the initiation of palliative care services for advanced cancer patients and is particularly low for patients with hematological malignancies. There is an urgent need to better understand the underlying causes and to develop multilevel methods to improve earlier integration of PPC services into the care of children with cancer.

Conflicts of Interest

The authors have no conflicts of interest.

Data Availability Statement

The data are not publicly accessible as it contains information that could compromise patients privacy.

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