

RESEARCH ARTICLE

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The Do-Not-Resuscitate Order for Children With Terminal Cancer Admitted to a Palliative Care Unit

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ABSTRACT

Introduction: Research on do-not-resuscitate (DNR) orders mainly focuses on adult patients, with only a few studies investigating children. We aimed to investigate the use of DNR orders and factors associated with the signing of a DNR order among children with terminal cancer in mainland China.

Methods: This study was a retrospective analysis involving children with terminal cancer who died in the palliative care unit of a large-scale tertiary teaching hospital in western China between July 31, 2015, and August 31, 2021. The DNR order information, demographics, and disease-related characteristics of admitted children were analyzed.

Results: All DNR orders were signed by the children's legal guardians, mainly within 3 days of death. The time to signing a DNR order was associated with disease severity, prior antitumor treatment, and overall survival time. The most common symptoms in these children were pain, restlessness, and dyspnea. Most of them had multiple distressing symptoms.

Conclusions: Our findings indicate that the DNR order is highly accepted by the families of children receiving palliative care, but very few children receive palliative care services in mainland China. It is necessary to improve palliative care for children and develop clearer guidelines to standardize DNR practices in mainland China.

1 | Introduction

Childhood cancer carries a significant disease burden, with almost 400,000 cases diagnosed globally every year [1]. Although antitumor treatments have achieved good objective tumor response rates and improved the overall survival of patients, approximately 20% of children diagnosed with malignant tumors still die [2, 3]. Children usually suffer from multiple symptoms at the end of life, such as pain, fatigue, and restlessness. Considering physical and mental immaturity, the distress experienced by children may be more severe than that experienced in adults [4–6], seriously impairing the quality of life of the children and

their families [7]. It is the responsibility of healthcare providers to provide adequate symptom control for children during their final phase of life. When death is imminent and all therapeutic modalities have been exhausted, unnecessary suffering should be avoided, and a do-not-resuscitate (DNR) order can be offered [8].

A DNR order is a written medical directive that indicates the refusal of cardiopulmonary resuscitation (CPR) following sudden cardiac or respiratory arrest [9]. In some cases, CPR can resuscitate children whose heartbeat and breathing have stopped, but for children with advanced tumors, rescue before the end of life not only extends survival time but also prolongs discomfort

Na Li and Duan Guo contributed equally to this work.

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and distress. The DNR is commonly considered and documented within the framework of palliative care. Determining the status of the DNR order helps formulate the best supportive treatment plan for children at the end of life, focusing on controlling the suffering of the child and protecting their dignity and avoiding the waste of medical resources and the additional physical and mental suffering caused by excessive and futile medical treatments [9, 10].

In China, the Hospice Palliative Care Act was signed and enacted on June 7, 2000 [11, 12]. The legislation states that end-stage patients are allowed to die naturally, which includes them signing a DNR order before the end of life. In Hong Kong, doctors sign DNR orders after assessing a patient's best interests [13]. The rate of DNR orders for patients in Hong Kong at the end of the study period was 94.7% [14]. In mainland China, Ms. Diandian Luo has advocated for death with dignity and an advance directive and founded a public welfare website emphasizing choice and dignity and allowing patients to register and fill out treatment-related options.

The DNR order has existed in various forms for over 50 years [15]. With social progress and improvements in medical levels, the decision to refuse CPR before death has become increasingly accepted. However, available research on DNR orders mainly focuses on adult patients, with only a few studies investigating children. To date, no study in mainland China has reported DNR orders in children. The potential reason may be that death is a taboo subject in traditional Chinese culture, and there are still no laws regulating DNR signing in mainland China.

To address this research gap, we aimed to investigate the use of DNR orders and the factors associated with the timing of DNR order signing among children with advanced cancer receiving palliative care in mainland China. The results may provide a better understanding of the needs of children at the end of life and their families and improve the quality of palliative care and children's quality of life.

2 | Materials and Methods

2.1 | Study Design and Population

A retrospective analysis was performed using the electronic medical records to identify children who died in the palliative care unit of a large-scale tertiary teaching hospital in western China between July 31, 2015, and August 31, 2021. The inclusion criteria were patients less than 18 years of age with a pathologically confirmed malignant tumor who died in the palliative care unit. The exclusion criteria were children with early-stage cancer who died from noncancer-related causes or had incomplete medical or nursing records.

2.2 | Data Collection

The palliative care department director approved the acquisition of patient data. The patients' electronic data were obtained from the hospital's information system and were retrieved by a dedicated medical record department administrator. We conducted a statistical analysis of the children's demographic and medical information, including age, sex, disease type, tumor metastasis, length of stay, reason for admission, prior antitumor treatment, survival time, and DNR order status.

Consent for CPR refusal, including chest compression, endotracheal intubation, and assisted mechanical ventilation, was regarded as a DNR order.

2.3 | Statistical Analysis

DNR order information and demographic and disease-related characteristics were analyzed using descriptive statistics. The chi-squared test was used to identify statistically significant differences in demographics and cancer types between patients with and without DNR orders. $p < 0.05$ was considered significant. SPSS 25 (IBM, Armonk, NY, USA) was used for statistical analysis.

3 | Results

3.1 | Patient Characteristics

The 42 children who died in the palliative ward during the study period were included in the study. The patients' characteristics are summarized in Table 1.

3.2 | DNR Order-Signing Rates

Among the 42 children, 34 (81%) were found to have a DNR order signed before death. Of them, 22 (64.7%) were male, 12 (35.3%) were female, 24 (70.6%) were younger than 12 years, and 10 (29.4%) were 12 years or older. Among the children with a DNR order, 11 (32.3%) had central nervous system tumors, five (14.7%) had hematological tumors such as leukemia and lymphoma, five (14.7%) had head and neck tumors, four (11.8%) had skin or digestive system tumors, three (8.8%) had urogenital tumors, and one (2.9%) had a bone or gynecological tumor. In the last month of life, 11 (26.2%) children had been treated with antitumor therapy; among them, 81.8% had DNR orders (Table 1).

3.3 | The Time of Signing a DNR Order

Of the 34 guardians of children with a DNR order, 30 (88.2%) signed it within 3 days before death, and 14 (46.7%) signed it on the day of death. Three guardians (8.8%) signed the DNR order from 4 days to 2 weeks before the child's death, and only one (3%) signed it over 2 weeks before death (Figure 1). The median time between the signing of the DNR order and death was 1 day (range: 0–21 days), with an average interval of 1.8 ± 3.88 days.

3.4 | The Person Who Signed the DNR Order

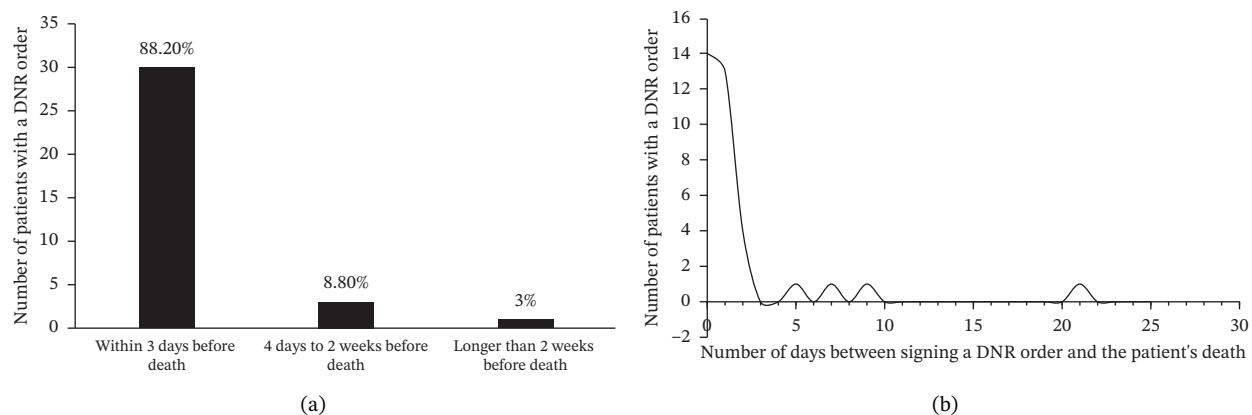
The children's legal guardians signed all DNR orders. The guardians of the children were mainly fathers (19/34, 55.9%) and mothers (13/34, 38.2%); only one was the child's sister, and the other was staff at the welfare institution (because the child was an orphan). There was no significant difference in the DNR order-signing individual between children over 12 years old and those 12 years old or younger (Figure S1).

3.5 | Reasons for Admission

Most of the 42 children were hospitalized because of tumor complications. Among them, 15 had infections, most commonly pulmonary infections. Two children had respiratory

TABLE 1 | Demographic and disease-related characteristics among patients with or without a DNR order.

Participants	Entire population, <i>n</i> (%)	Signed DNR order		<i>p</i> value
		With, <i>n</i> (%)	Without, <i>n</i> (%)	
Median age, y (range)	42 (100)	34 (81)	8 (19)	0.8037
< 12 y of age	12 (1–18)			
≥ 12 y of age	30 (71.4)	24 (80)	6 (20)	
Sex	12 (28.6)	10 (83.3)	2 (16.7)	0.2096
Male				
Female	29 (69)	22 (78.1)	7 (21.9)	
Primary cancer type	13 (31)	12 (92.3)	1 (7.7)	0.2354
Central nervous system				
Hematology	16 (38.1)	11 (68.8)	5 (31.2)	
Head and neck	7 (16.7)	5 (71.4)	2 (28.6)	
Gastrointestinal	5 (11.9)	5 (100)	0 (0)	
Skin and soft tissue	4 (9.5)	4 (100)	0 (0)	
Genitourinary	4 (9.5)	4 (100)	0 (0)	
Gynecology	3 (7.1)	3 (100)	0 (0)	
Gynecological	1 (2.4)	0 (0)	1 (100)	
Bone	1 (2.4)	1 (100)	0 (0)	
Oncologic therapy during the last month of life	1 (2.4)	1 (100)	0 (0)	
No				
Yes	31 (73.8)	24 (77.4)	7 (22.6)	
	11 (26.2)	9 (81.8)	2 (18.2)	

**FIGURE 1** | The time interval between signing the DNR orders and death ($n = 34$). (a) Most DNR orders were signed when the children were near death. The longer they were away from death, the fewer DNR orders their legal guardians signed. (b) Most DNR orders (30/34, 88.2%) were signed within 3 days before death. In three patients (8.8%), the orders were signed from 4 days to 2 weeks before death. In only one child (3%), the order was signed over 2 weeks before death.

failure at admission, one had septic shock, and 10 were hospitalized due to intracranial hypertension (most of whom suffered from central nervous system and head and neck tumors). Five children had a consciousness disorder on admission, which was considered to be caused by intracranial hypertension, abnormal liver and kidney function, and hepatic encephalopathy. The others were admitted due to intestinal obstruction and lower limb paralysis. The median time to receive palliative care was 7 days, and the average time was 11.5 days. Most of the children were hospitalized in our

palliative care unit for the first time, except for five children who were hospitalized multiple times due to pain.

3.6 | Symptoms on Admission

The most common admission symptom of children was pain (37/42, 88.1%), followed by restlessness (16/42, 38.1%), dyspnea, and vomiting (13/42, 31%). Children with convulsions and coughs accounted for 11.9% (5/42). In addition, four children had nausea (4/42, 9.5%), and two children (2/42, 4.8%) had recurrent edema

(Figure 2). Among the 42 patients, 50% admitted to the palliative care unit had three or more symptoms, 38.1% had two main symptoms, and 11.9% had only one (Figure S2).

3.7 | Past antitumor treatment status of the children

Nine (9/12, 75%) of the 12 (12/42, 28.6%) children who had received antitumor treatment 3 months before death had a DNR order. Among the 11 children (11/12, 91.7%) who received antitumor treatment 1 month before death, nine (9/11, 81.8%) had a DNR order. Among the 11 children (11/42, 26.2%) who received antitumor therapy 3–6 months before death, 9 (9/11, 81.8%) had a DNR order. In addition, 22 (22/24, 91.7%) of the 24 children (24/42, 57.1%) who received antitumor therapy more than half a year before death had a DNR order (Figure 3). Therefore, the longer the interval between antitumor treatment and death, the higher the rate of DNR orders.

3.8 | The Relationship Between Overall Survival Time and Signing the DNR Order

Among the 42 children, the median overall survival time was 10 months (range: 10 days–8 years). Six (14.3%, 6/42) children had a total survival of less than 1 month; six had a survival of 1 month or more but less than 3 months; and six had a survival of 3 months or more but less than 6 months. Among those three groups, 66.7% (4/6) had a DNR order, but 33.3% (2/6) did not. Among the six children with a survival longer than 6 months and less than 1 year, 83.3% (5/6) had a DNR order, but 16.7% (1/6) did not. Among the eight children with a survival of 1–2 years, 87.5% (7/8) had a DNR order, while 12.5% (1/8) did not. Among the seven children with a survival of 2 years or more, 100% had a DNR order (Figure 4(a)). As overall survival time increased, the proportion of legal guardians signing DNR orders also increased (Figure 4(b)).

3.9 | Resuscitation Before Death Among Children Who Have Not Signed the DNR Order

In our study, eight children who did not have a DNR order were resuscitated before death. All patients underwent drug resuscitation, and four of them were placed on ventilators. Among them, one child had endotracheal intubation, and two were rescued by chest compression (Figure S3A). Most families choose the less traumatic method when signing the DNR order. Despite a series of resuscitations, the survival time of the children did not increase. The time from the beginning of resuscitation to death was less than 1 h for most children, and only one child survived for more than 1 day after resuscitation (Figure S3B).

4 | Discussion

4.1 | Main Findings/Results of the Study

To the authors’ knowledge, this study is the first to report on the use of DNR orders for children with terminal cancer in mainland China, filling a research gap on DNR in China. Although only 42 children were included, this study provided a detailed analysis of DNR orders, including the DNR order–signing rate, time, and associated factors. The results indicated that there was an

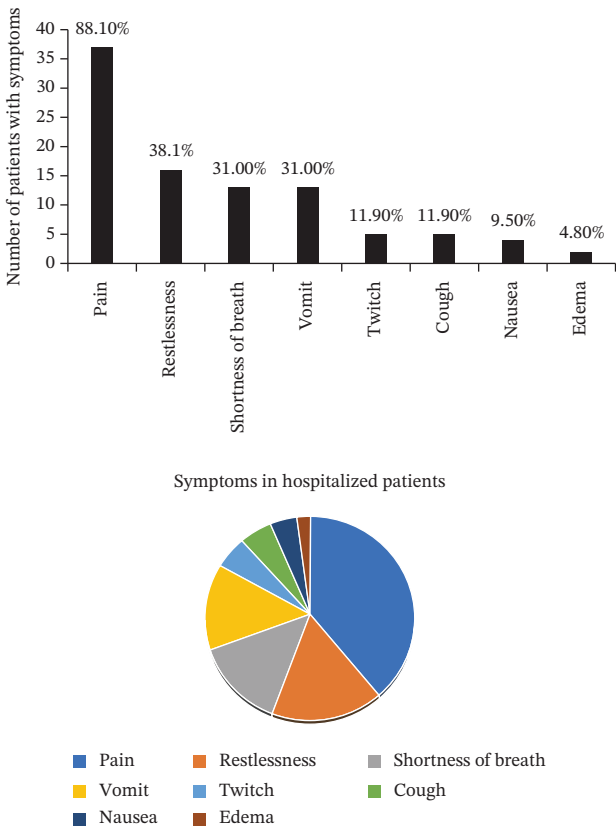


FIGURE 2 | Symptoms at admission (n = 42): 37 (88.1%) had pain, 16 (38.1%) were restless, 13 (31%) had dyspnea, 13 (31%) had vomiting, five (11.9%) had convulsions, five (11.9%) had cough, four (9.5%) had nausea, and two (4.8%) had edema.

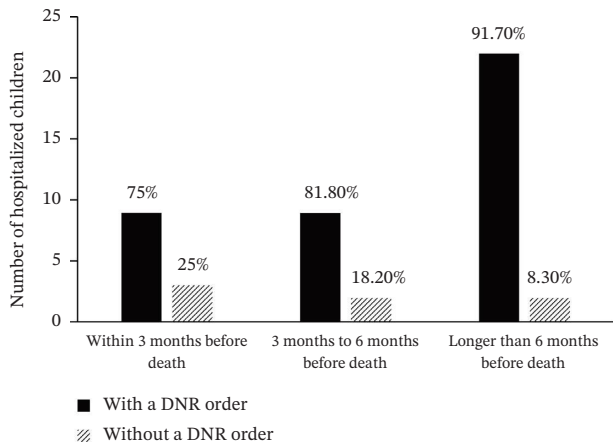


FIGURE 3 | DNR orders signed by the children who had received antitumor treatment in the past (n = 42). Twelve children (12/42, 28.6%) had received antitumor treatment 3 months before death. Among the 11 children (11/12, 91.7%) who received antitumor treatment 1 month before their death, nine (9/11, 81.8%) had a DNR order. Among the 11 children (11/42, 26.2%) who received antitumor therapy 3–6 months before death, 9 (9/11, 81.8%) had a DNR order. In addition, 22 (22/24, 91.7%) of the 24 children (24/42, 57.1%) who received antitumor therapy more than half a year before death had a DNR order.

obvious need for a DNR order document for children with advanced cancer admitted to a palliative care unit in mainland China, which could provide a basis for further investigation and

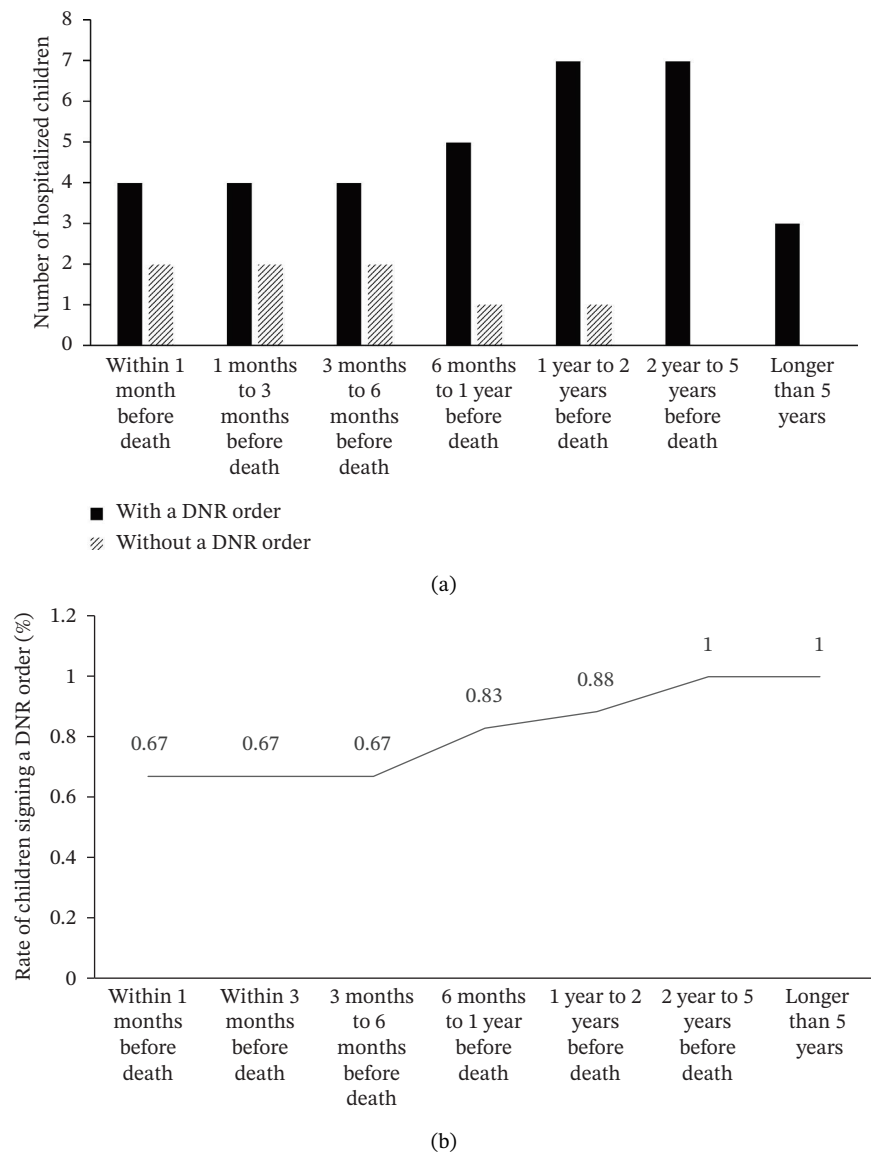


FIGURE 4 | All hospitalized children were grouped according to their survival ($n = 42$). (a) Six (14.3%, 6/42) children had a total survival of less than 1 month, six had a survival longer than or equal to 1 month and less than 3 months, and six had a survival longer than or equal to 3 months and less than or equal to 6 months. Among those three groups, 66.7% (4/6) had a DNR order, but 33.3% (2/6) did not. Among the six children with a survival longer than 6 months and less than 1 year, 83.3% (5/6) had a DNR order, but 16.7% (1/6) did not. Among the eight children with a survival of 1–2 years, 87.5% (7/8) had a DNR order, while 12.5% (1/8) did not. Among the seven children with a survival of 2 years or more, 100% had a DNR order. (b) As the overall survival time increased, the proportion of children's surrogates signing DNR orders also increased.

promote the development of laws regulating DNR orders for children.

4.2 | What This Study Adds

In our study, the DNR order–signing rate was 81%, which was higher than in previous studies. In the study by Chang et al. [16], among 225 pediatric patients who died of various tumors, only 57.8% had a DNR order before death. In the study by Bilal et al. [17], this figure was 70.9%, which is still lower than in our study (81%). The difference in DNR order–signing rates may partly be due to differences in study settings. The present study was conducted in a palliative care unit, while the other two studies were not. There is limited awareness of palliative care among the general public in mainland China [18]. Although approximately

25,000 children aged 0–14 years in mainland China were diagnosed with cancer in 2018 [19], few children with cancer were referred to specialist palliative care. Although a DNR order specifically instructs that CPR should be withheld in the event of cardiac or respiratory arrest, it is usually considered within the broader, active framework of palliative care, focused on symptom control, psychosocial support, and goal-concordant treatment—so DNR status should not be interpreted as the withdrawal of all medical care. Despite the fact that early palliative care has been demonstrated to significantly improve the quality of life compared with standard care, palliative care is still the last choice for children with terminal cancer in mainland China. Therefore, the children and their families admitted to palliative care units often experience higher levels of distress and feel more hopeless toward antitumor treatment than those in other

healthcare settings, which makes it easier for children's families to understand death and accept DNR. Additionally, the goal of palliative care is to provide end-of-life care and a good death [20]. The discussions of death between palliative care staff and children's families are common in palliative care units, which may also have a positive effect on attitudes of children's families toward the DNR order.

Although the DNR order–signing rate was high in our study, the median time from DNR order signing to death was short and similar to that in previous studies. A review of the literature revealed that the time between signing a DNR order and death was usually within 3 days [21]. In the study by McCallum et al. [22], the average duration was less than 24 h. In the study by Chang et al. [16], the interval was 2 days (range: 0–88). All of the above findings suggest that the DNR orders are always signed late. A possible reason for these misunderstandings is family members' confusion about writing a DNR order. They might mistakenly interpret DNR as an order for no life-extending medical treatments and interventions after the order is written, thus not consenting to DNR unless children are imminently dying. In fact, several previous studies revealed that patients with delayed DNR orders had higher mortality, longer length of stay, and higher total costs than admission DNR patients, while early DNR orders were associated with less aggressive procedures and more comfort measures [23–25]. Therefore, it could be better for doctors to discuss the DNR order with the legal guardians of the sick children as early as possible despite the association with dissatisfaction and aggravated psychological trauma, and not when the children are dying. Certainly, public education on palliative care and death is also essential.

Children with advanced cancer frequently experience significant physical symptoms and psychosocial distress that may be one reason for the DNR decision by their legal guardians. In the study by Zeng [26], the most common symptoms of children with advanced tumors were fatigue (93.7%), pain (87.3%), and loss of appetite (76.1%). Pain and fatigue were the most frequent and earliest symptoms, respectively. Here, the most common symptom of the included children was pain (88.1%). Cancer pain is complex and often multifactorial at the end of life, which makes pain management difficult in a high proportion of children with terminal cancer [27]. Pain can lead to increased stress, anxiety, and depressive symptoms, as well as decreased quality of life for children and their families, which would make them choose DNR [28]. In addition, we observed a high incidence of symptoms, including vomiting, nausea, and restlessness. Those symptoms could be related to the high percentage of children with intracranial hypertension and central nervous system tumors included in our study. The frequency of dyspnea was also relatively high. It may be that 35.7% of the children had infections at admission, mainly pneumonia. Severe cases developed respiratory failure and septic shock upon hospital admission.

A recent study investigating the symptomatic factors associated with DNR orders in adult patients with advanced cancer showed that dyspnea was independently associated with signing a DNR order [29]. It can partly explain the high DNR order–signing rate in our study. Regrettably, due to the small sample size, it is difficult to analyze the relevance of individual symptom factors to DNR orders. Further studies are warranted. Among the 42 children included, 88.1% (37/42) had received at least one

antitumor treatment, including surgery, chemotherapy, radiotherapy, targeted therapy, immunotherapy, and other treatments. However, as the disease progressed and pediatric patients got closer to death, antitumor treatments were reduced. As previously reported [30, 31], antitumor treatment leads to obvious side effects in pediatric patients and imposes numerous burdens on families that cause varying degrees of distress. The results also demonstrated that the longer the interval between antitumor treatment and the death of the children, the easier it was for their legal guardians to sign the DNR order. Possible reasons include the long-term burden on caregivers, the substantial economic burden on the families, the acceptance of the disease, and the feeling of a medically hopeless situation.

Moreover, we analyzed the resuscitation status of children without a DNR order. The results revealed that resuscitation before death did not prolong the survival of children with advanced tumors. In contrast, the inpatient care interventions prolonged the suffering of the children and wasted costly and strained healthcare resources.

Nevertheless, there are clinical situations in which a DNR order is signed before the patient has been referred to a palliative care or hospice facility. Whether a DNR order is signed should not be interpreted as causally linked to referral to palliative or hospice services. However, the present study specifically focused on DNR signing within a dedicated pediatric palliative medicine unit because of the particularities of pediatric patients. Some families come to the authors' institution as a last resort and, in reality, have not truly accepted palliative or hospice care. It can lead to parents being conflicted and reluctant to sign a DNR order or to signing and later retracting consent. It represents the most significant peculiarity and practical challenge when compared with adult DNR practice.

4.3 | Strengths and Weaknesses/Limitations of the Study

Our study provides the first descriptive information about DNR orders for children with terminal cancer in mainland China. This study was conducted in the palliative care unit of West China Fourth Hospital of Sichuan University, which is the first pediatric palliative care program in Sichuan Province and one of the most established and comprehensive in China. Therefore, our research is innovative and has some reference value.

Of course, the present study still has some limitations. First, it was a single-center study with a small sample size, and the statistical analysis may have had limited power. The small sample size is explained by the fact that palliative care and hospice care are still at an early stage of development in China, and public awareness of palliative care and hospice care is limited. In addition, constrained by traditional cultural attitudes and limited public understanding, parents seldom send children to specialized palliative or hospice facilities. Restrictions on the professional scope of practice also mean that ordinary palliative or hospice institutions are often unable to admit pediatric patients. Our institution was one of the earliest domestic centers to establish palliative and hospice services, so we have clinical experience with pediatric cases, but the number of cases remains limited. We are now conducting a second phase study to collect pediatric DNR and other related data nationwide to strengthen and expand our findings. Second,

given its retrospective nature, only data in the patient charts could be analyzed, preventing the identification of factors associated with DNR orders. Furthermore, the study was cross-sectional, which implies that causality cannot be concluded. Third, there was probably a selection bias owing to enrollment being restricted to a palliative care service. Clinicians may issue DNR orders without referring patients to specialist palliative care, and this study may lose sight of DNR orders outside palliative care. In addition, given the differences in socioeconomic status and culture across China, it would be challenging to extrapolate the results to other cities. Moreover, a huge disparity in palliative care acceptance is expected between urban and rural populations. Further multicenter, larger-scale research is needed to deepen our understanding of DNR orders in children with end-stage disease.

5 | Conclusion

This study showed that among children with advanced cancer admitted to a palliative care unit in western China, the signing rate of DNR orders was relatively high, and most DNR orders were signed around the time of death. In addition, children with terminal cancer often face a significant symptomatic burden, but only very few children receive specialist palliative care in mainland China. The findings suggest that public education on palliative care, DNR orders, and death is essential. Palliative care, especially in children, appears to require improvement in mainland China. Meanwhile, regarding ethical and legal issues, it may be necessary to develop clear guidelines to standardize DNR practices in mainland China.

Author Contributions

Na Li and Duan Guo conducted the studies, collected data, and drafted the manuscript. Na Li and Jianjun Jiang performed the statistical analysis and participated in its design. Na Li and Qian Deng participated in the acquisition, analysis, or interpretation of data and in drafting the manuscript.

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Disclosure

All authors read and approved the final manuscript.

Ethics Statement

The study was carried out after approval by the Medical Ethics Committee of West China Fourth Hospital of Sichuan University (HXSJ-EC-2024004). The authors confirm that all methods were performed in accordance with the relevant guidelines. All procedures were performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments, and informed consent was obtained from all participants.

Consent

Please see the Ethics Statement.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

All data generated or analyzed during this study are included in this published article.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.

Supporting Information 1. Figure S1 The person who signed the DNR order by age group ($n = 34$). All DNR orders were signed by the children's legal guardians; 19 (55.9%) DNR orders were signed by the children's fathers, 13 (38.2%) by the mothers, and two (5.9%) by a sister or others. There were no significant differences in the DNR order-signing individual between children over 12 years old and those 12 years old or younger.

Supporting Information 2. Figure S2 How many symptoms the children had at admission ($n = 42$). 5/42 (11.9%) children had only one symptom, 16/42 (38.1%) had two, and 21/42 (50%) had more than three.

Supporting Information 3. Figure S3 Resuscitation measures adopted by the children who had no DNR orders ($n = 8$). (a) Eight (8/8, 100%) children were resuscitated with drugs, four (4/8, 50%) were resuscitated with ventilators, and two (2/8, 25%) were resuscitated with chest compression. (b) Most children (5/8, 62.5%) died within 1 h after resuscitation, two children (2/8, 25%) died from 1 h to 1 day after resuscitation, and only one child (12.5%) died more than 1 day after resuscitation.