Withdrawing treatment of Children in the pediatric intensive care unit of a China Children’s Hospital: A Single Center Years Retrospective Analysis

CURRENT STATUS: UNDER REVIEW

Huaqing Liu
Health supervision institute of gusu district, suzhou

Dongni Su
Soochow University Affiliated Children's Hospital

Xubei Guo
children's hospital of soochow university

Yunhong Dai
children's hospital of soochow university

Xingqiang Dong New
Soochow University Affiliated Children's Hospital

Qiujiao Zhu
children's hospital of soochow university

Zhengjiang Bai
children's hospital of soochow university

Ying Li
children's hospital of soochow university

Shuiyan Wu doctorwu1219@sina.com
Soochow University Affiliated Children's Hospital

Corresponding Author
ORCID: 0000-0002-8963-5082

DOI:
10.21203/rs.2.24029/v1

SUBJECT AREAS
Medical Ethics

KEYWORDS
Withdrawing treatment Premature withdrawing Children Pediatric intensive care unit
Abstract

Background: Published data and practice recommendations on end-of-life generally reflect Western practice frameworks, there are few reports that refer to withdrawing treatment of children in China.

Methods: Withdrawing treatment and reasons of children in the pediatric intensive care unit (PICU) of a regional children's hospital in eastern China from 2006 to 2017 was studied retrospectively. Withdrawing treatment was divided into medical withdrawing and premature withdrawing as defined.

Results: The incidence of withdrawing treatment among children in the PICU decreased significantly, for premature withdrawing from a 3-year average of 15.1% in 2006–2008 to 1.9% in 2015–2017 (87.4% reduction). The decrease in cases of premature withdrawing contributed most of the decrease in total withdrawing. The median age of children in whom treatment was withdrawn increased from 14.5 (interquartile range: 4.0–72.0) months in 2006 to 40.5 (interquartile range: 8.0–99.0) months in 2017. Reasons given by guardians of children whose treatments were withdrawn in 2011–2017, “illness is too severe” ranked first, accounting for 66.3%, followed by “condition has been improved” (20.9%). Only a few of the guardians ascribed withdrawing treatment to economic reasons.

Conclusions: The decreasing in incidence of withdrawing treatment and an increase in the age of children whose treatment was withdrawn show that guardians are more willing to actively treat their children in this children's hospital during the last years. Chinese children's guardians have their own unique ways of expression when self-reported reasons for withdrawing treatment.

Background

It is an inevitable dilemma for parents and physicians to withdraw treatment in critically ill
children. Published data and practice recommendations on end-of-life generally reflect Western practice frameworks [1, 2]. In regions with different social cultures, religions, ethnicities, health care levels, and economic development, people often have different attitudes toward withdrawal of treatment. Even in the same region, there are controversial opinions regarding withdrawing treatment [1, 3, 4]. China has the largest number of children in the world, with 220 million children aged 0-14 years [5]. The Chinese government implemented the Children's Development Program of China (2011–2020) in 2011 with the aim to reduce the mortality of infants and U5MR to < 10‰ and 13‰, respectively [6]. Five years after implementation of the program, the interim statistical monitoring report showed that the infant mortality rate and the U5MR were reduced by 5‰ and 5.7‰ compared to 2010, respectively [7]. However, the report did not provide the statistical data pertaining to withdrawing treatment in critically ill children, which would have contributed to infant mortality and U5MR, and studies on treatment abandonment in pediatric intensive care units (PICUs) in China are lacking.

There is currently no relevant legislative provision in China for withdrawing treatment [8]. Due to the special relationship between physicians and patients and the lack of related laws, whether or not to withdraw treatment is often decided by the child’s guardians, although these decisions may not be in the best interest of the child. Key decisions may include whether or not to use antibiotics in the instance of life-threatening infections and cardiopulmonary resuscitation in the event of cardiac arrest or to escalate to emergency or intensive care settings if the child becomes unstable [9]. In the past few decades, economic, healthcare, and social conditions in China have changed significantly. To better understand withdrawal of treatment in China, we report the associated data at a regional children's hospital in eastern China during the last years.

Methods
1 Study subjects

The study was approved by the hospital ethics committee. All children were studied following written informed consent given by their parents. The study included pediatric patients who were admitted to the PICU of the Children's Hospital of Soochow University from 2006 to 2017. The hospital is the only third-grade class-A hospital in Suzhou and the major hospital to admit and treat critically ill children in the region. The inclusion criteria included the following: (1) met PICU admission standards and treated in the PICU; and (2) children whose treatments were withdrawn. The exclusion criteria were as follows: (1) admission to the PICU, but subsequently transferred to the general wards or departments; (2) > 14 years of age; (3) in a near-death state and treatment was abandoned at the time of admission; and (4) children with brain death.

2 Definition of withdrawing treatment

Withdrawing treatment was divided into two categories, defined as follows: (1) medical withdrawing: the child was in a permanent, irreversible coma or inevitable dying condition, treatment in a child for whom pursuing treatment was futile, and the guardian requested the medical staff to limit or withdraw life-sustaining treatment; (2) premature withdrawing: also was defined as treatment abandonment, guardian refusal for active treatment of a severely ill child for which treatment was indicated or for which there was some chance of survival, including the following situation, (a) the guardian took the child from the hospital and did not state the reason(s), (b) the child was still severely ill and the guardian did not authorize any medical treatments or partial treatments and requested for discharge for other reasons.

3 Data collection and reporting of reasons for withdrawing.

The age, gender, place of residence, type of disease, length of stay in the PICU, and condition at the time of discharge were collected from the hospital database (data for
2013 and 2014 were not available). Data on the condition of the child and the withdrawn treatment were collected from the "informed consent" and "doctor-patient conversation record" documents. These documents also recorded the guardian’s self-reported reason for abandoning the child’s treatment since 2011.

4 Statistical analyses

Age and days in ICU are expressed as the median and interquartile range (IQR). A Wilcoxon two-sample test was used for comparison of age and days in ICU between two groups. Categorical variables are expressed as a frequency (%), and a chi-square test or Fisher exact test was used for inter-group comparisons. A trend test was used for analyzing the change in the incidence of withdrawing treatment across time from 2007 to 2017. SAS 9.3 was used for data processing and statistical analyses. All tests were two-tailed and a \( p < 0.05 \) was considered statistically significant.

Results

1 General characteristics of the children and incidence of withdrawal of treatment

From 2006 to 2017 (excluding 2013 and 2014), a total of 8006 children were admitted to the PICU; treatments were withdrawn in 680 children, including medical withdrawing in 174 children and premature withdrawing in 506 children. The general characteristics of children whose treatment was withdrawn are shown in Table 1. The age of children who experienced medical withdrawing was significantly higher than those who experienced premature withdrawing (median: 24 vs. 8 months, \( p < 0.001 \)). There was significant difference in primary disease between children who experienced premature withdrawing and medical withdrawing (infectious proportion: 20.7 vs. 35.6%, \( p < 0.001 \)).
The year-incidence curve is shown in Fig. 1A. The highest incidence of total withdrawing treatment (24.3%) and the highest incidence of premature withdrawing (20.6%) occurred in 2007. The incidence of total withdrawing treatment and premature withdrawing followed a year-by-year decreasing trend from 2007 to 2017 (p < 0.01). Incidence of total withdrawing treatment dropped from its highest point (24.3%) in 2007 to its lowest point (2.6%) in 2017, the 3-year average incidence dropped from 17.5% in 2006–2008 to 4.0% in 2015–2017 (a 77.1% reduction). The 3-year average incidence of premature withdrawing dropped from 15.1% in 2006–2008 to 1.9% in 2015–2017 (a 87.4% reduction). The proportion of premature withdrawing in all children whose treatment was withdrawn declined from 88.0% in 2006 to 43.5% in 2017 (Fig. 1B). The decrease in cases of premature withdrawing contributed most of the decrease in total withdrawing.

The median age of children is shown in Fig. 2. There was a downward trend in the median age of all children before 2009, but this increased significantly each year from 2009; the median age increased from 4.0 months (IQR: 2–24) in 2009 to 40.5 months (IQR: 8–99) in 2017. The children who experienced medical withdrawing had a higher age increasing than those who experienced premature withdrawing.
2 Reasons given by guardians for withdrawing treatment and condition of children at the time of discharge.

Reasons given by guardians for withdrawing treatment are shown in Table 2. Among the 326 children whose treatments were withdrawn in 2011–2017, “illness is too severe” ranked first, accounting for 66.3%, followed by “condition has been improved” (20.9%). Almost all guardians (96.1%) of children who experienced medical withdrawing self-reported reason as “illness is too severe”, a few guardians (3.9%) self-reported reason as “condition has been improved”. For guardians of children who experienced premature withdrawing, these two reasons account for 46.7% and 32.0%, respectively. Of all guardians of children who experienced premature withdrawing, 7 (3.5%) guardians self-reported “economic reason”, one (0.5%) guardians self-reported “unclear diagnosis”.

Table 2

| Reasons                  | Total, n = 326,(%) | Medical withdrawing, n = 129,(%) | Premature withdrawing, n = 197,(%) | p* |
|--------------------------|--------------------|----------------------------------|-----------------------------------|----|
| Illness is too severe    | 216 (66.3)        | 124 (96.1)                       | 92 (46.7)                         | < 0.001 |
| Condition has been improved | 68 (20.9)      | 5 (3.9)                          | 63 (32.0)                         |    |
| Economic reason          | 7 (2.1)           | 0 (0.0)                          | 7 (3.5)                           |    |
| Unclear diagnosis        | 1 (0.3)           | 0 (0.0)                          | 1 (0.5)                           |    |
| Unstated reason          | 34 (10.4)         | 0 (0.0)                          | 34 (17.3)                         |    |

*p value for medical withdrawing vs. premature withdrawing.

There were 132 (40.5%) children who died following discharge, of which 98 deaths were classed as medical withdrawing and 34 deaths were premature withdrawing (mortality rate: 76.0 vs 17.3%, p < 0.001).

3 Treatment modalities that were withdrawn.

The life-sustaining treatment modalities that were withdrawn are shown in Table 3. The most frequent modalities withdrawn were intravenous, ventilation and intubation. In 24% of cases, all three treatment modalities were withdrawn.
| Treatments                  | Total, n = 680, (%) | Medical withdrawing, n = 174, (%) | Premature withdrawing, n = 506, (%) | p*     |
|-----------------------------|---------------------|-----------------------------------|-------------------------------------|--------|
| Intravenous                 | 437 (64.3)          | 103 (59.2)                        | 334 (66.0)                          | 0.106  |
| Ventilation                 | 279 (41.0)          | 105 (60.3)                        | 174 (34.4)                          | < 0.001|
| Intubation                  | 277 (40.7)          | 103 (59.2)                        | 174 (34.4)                          | < 0.001|
| Antimicrobial therapy       | 113 (16.6)          | 19 (10.9)                         | 94 (18.6)                           | 0.019  |
| Inotropic and vasopressors  | 70 (10.3)           | 7 (4.0)                           | 63 (12.5)                           | 0.002  |
| Dialysis                    | 25 (3.7)            | 8 (4.6)                           | 17 (3.4)                            | 0.454  |
| Transfusion of blood products| 21 (3.1)            | 3 (1.7)                           | 18 (3.6)                            | 0.228  |
| Nutrition                   | 9 (1.3)             | 3 (1.7)                           | 6 (1.2)                             | 0.701  |

*p value for medical withdrawing vs. premature withdrawing.

Discussion

Withdrawing treatment is not only a medical ethical issue, but a social issue. There has been considerable debate about how to implement withdrawal of treatment. Some scholars in China believe that withdrawal of treatment in ICUs should follow the principle of benefit and respect the patient's willingness and fairness principle [10]. People also believe that decisions on withholding/withdrawing treatment need to take account of the likely success, benefits, burdens and risks of treatment, as well as the patient's presumed wishes [4]. For children, however, withdrawing treatment is decided by their guardian(s), as children do not have full civil liability, and guardians' decisions are not always in the best interest of the child. Therefore, in this study we classified cases of withdrawing treatment into two categories: children who were unlikely to survive and whose treatment was withdrawn and children for whom a treatment was indicated but whose guardian(s) chose to abandon treatment.

For the treatment of children with severe illness in China, the general practice of physicians is to have a conversation with the child’s guardian, introduce the child's condition to the guardian, provide medical advice, including whether or not it is worth administering a treatment, and discuss treatment methods and prognosis, after which the
guardians are asked to make a decision. In many cases, even if a child has a chance to survive, their guardians choose to abandon treatment. When patients cannot articulate their wishes in American hospitals, it has been reported that ICU physicians and nurses usually leave final decisions in the hands of the families [11]. In the USA, physicians won’t say in absolute terms whether a child will die or whether they will experience poor functional outcomes [12], and fear of litigation is a major barrier to properly informing a child's guardians in Greece [13]. Physicians in China experience similar restraints. There are some official guidelines for withholding and withdrawing therapy for critically ill patients in some countries and regions [1, 14-17]. There’s no legal procedure and official guidelines for withdrawing treatment in China. In China, especially in the past decade, tension and deterioration of the doctor-patient relationship was increasing, there have been many disputes and contradictions between doctors and patients caused by patients' treatment choice, and even some medical staffs have suffered injuries from radical patients or patients' families. For instance, on October 3, 2016, a pediatrician in Shandong Province was killed by the father of a girl he had treated, and on December 24, 2019, a Beijing emergency physician was killed by a family member of a 95 year old patient with advanced cancer. In such a situation, in order to avoid the troubles caused by medical disputes, doctors will use more obscure technical terms to accurately describe patients' conditions in the process of communication between doctors and patients, although these technical terms may not be fully understood by patients and their families. For the prognosis evaluation and treatment of severe patients, doctors will become more conservative when discussing with patients or their families, especially in importunate patients or their families. This makes it difficult for this part of patients to obtain more active treatment opinions from doctors.

From the results presented in this study—over the past decade in the PICU, there has
been a decrease in incidence of withdrawing treatment and an increase in the age of children whose treatment was withdrawn—show that guardians are more willing to actively treat their children. It has been reported that guardians withholding or withdrawing intensive care for extremely preterm infants at the limits of viability has become more acceptable than it was 20 years ago in Germany, Switzerland, and Austria [18]. The incidence of withdrawing treatment in recent years in this study is similar to the incidence of withdrawing treatment of neonatal intensive care in Korea [19]. The frequency of PICU patients who undergo the process of withholding or withdrawing life-sustaining treatment was 1.5% in Chile from 2004 to 2014 [20]. Decisions on end-of-life care in neonates shifted from active resuscitation to non-active resuscitation in Korea between 2001 and 2015 [19]. In contrast, the proportion of non-active resuscitation for critically ill children in China is declining. There are several possible reasons for the change in the attitude of the guardians of critically ill children toward withdrawing treatment. The economic status of children's families has improved over the past decade and families are, therefore, more capable of paying medical expenses. It is interesting to note that a short economic crisis broke out in China between 2007 and 2008, and the incidence of withdrawing treatment especially premature withdrawing reached a peak in 2007. Indeed, economic factors are key in deciding whether or not to abandon treatment [21]. Other studies have also shown that per capita GDP has a high negative correlation with infant mortality in China [22]. In this study, more than one-half of the guardians stated that their reason for withdrawing treatment was that the child's condition was too severe. Only a few of the guardians ascribed withdrawing treatment to economic reasons, which is inconsistent with another study in which economic reasons accounted for one-half of the total [23]. This difference may be due to variations in the study method. Our medical documents only recorded guardians’ self-reported reasons for treatment withdrawal, which may have introduced a
bias. Children at the time of withdrawal of treatment had lower disease severity than at admission [23], and one in five guardians cited “condition has been improved” as a reason for withdrawing in this study, of most these guardians were guardians of children who experienced premature withdrawing. We suggest that this was not representative of the true reason for withdrawing treatment, guardians may have moderated their statements to alleviate their guilt. Under the influence of Chinese Confucian culture, guardians are used to the expression of compromise. We believe that the main reasons for premature abandonment may be related to economic status and uncertainty of prognosis. Children are often only covered by limited health insurance, and continuing treatment will incur a heavy economic burden. We observed another phenomenon that premature abandonment was rare in children raised in social welfare institutes, in large part because the treatment expenses of such children are ensured by the government.

Although death practices are changing in China, the idea of a death occurring at home or in the person’s hometown, in the main hall in the presence of ancestor tablets is still cherished [3]. This may be one of the factors affecting the guardian’s decision. The low proportion of deaths in hospital of children whose treatment was withdrawn prematurely and the fact that some children experiencing medical withdrawing survived when discharged from hospital may be influenced by the death culture in China. Similar practices can be observed elsewhere: home deaths for critically ill babies/children does occur in the UK, although infrequently [24]. When interpreting the results from this study, some limitations should be considered. This was a single center retrospective study. The region where the hospital is located is undergoing rapid urbanization, and is an economically developed region in China. The results of this study are not representative of all of China. The impact of culture, healthcare insurance status, religion and education on the withdrawal of treatment has not been studied.
Conclusions

The decreasing in incidence of withdrawing treatment and an increase in the age of children whose treatment was withdrawn show that guardians are more willing to actively treat their children in this children’s hospital during the last years. Chinese children's guardians have their own unique ways of expression when self-reported reasons for withdrawing treatment.

Abbreviations

PICU, pediatric intensive care unit;
USMR, mortality ratio in children under 5;
IQR, interquartile range.

Declarations

1) Acknowledgements

Not applicable.

2) Authors' contributions

HQ L: Analyzed the data and drafted the manuscript; DN S: Collected clinical data and participated in analyzing the part of data; XB G and YH D: Collected clinical data; QJ Z: Participated in communicating with patients’ guardians; ZJ B, XQ D and YL: Participated in the discussion and interpretation of the data and results; assessed clinical prognoses of patients; SY W: Designed the research, involved in the critical revision of this manuscript and participated in the discussion and interpretation of the data and results; assessed clinical prognoses of patients. All authors have read and approved the manuscript.

3) Funding
Design of the study and collection, analysis, and interpretation of data and in writing the manuscript were funded by Suzhou Science and Technology Development Project (project code: SYS 201757) and the Natural Science Fund for colleges and universities of Jiangsu Province (project code: 18KJB320022).

4) Availability of data and materials
The datasets used and/or analysed during the current study are available from the corresponding author (Shuiyan Wu) on reasonable request.

5) Ethics approval and consent to participate
All procedures performed in studies involving human participants were in accordance with the ethical standards of the Children’s Hospital of Soochow University and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. All participants were enrolled following written informed consent given by their parents and the permission to access patient data was obtained from the health facility. Data on the condition of the child and the withdrawn treatment were collected from the informed consent form and the doctor-patient records. These documents also recorded the guardian’s self-reported reason for abandoning the child’s treatment since 2011. The use of this data was approved by the ethics committee.

6) Consent for publication
Not applicable.

7) Competing interests
The authors declare that they have no conflict of interest.

8) Author details

1 Children’s Hospital of Soochow University, Suzhou, Jiangsu, 215000, The People’s Republic of China.
2 Health Supervision Institute of Gusu District, Suzhou, Jiangsu, 215000, The People's Republic of China.

References

1. Wong WT, Phua J, Joynt GM. Worldwide end-of-life practice for patients in ICUs. Curr Opin Anaesthesiol. 2018;31:172-8.

2. Yazigi A, Riachi M, Dabbar G. Withholding and withdrawal of life-sustaining treatment in a Lebanese intensive care unit: a prospective observational study. Intensive Care Med. 2005; 31:562-7.

3. Setta SM, Shemie SD. An explanation and analysis of how world religions formulate their ethical decisions on withdrawing treatment and determining death. Philosophy, Ethics, and Humanities in Medicine. 2015;10:6.

4. Choudry M, Latif A, Warburton KG. An overview of the spiritual importances of end-of-life care among the five major faiths of the United Kingdom. Clinical Medicine. 2018;18:23-31.

5. Tabulation on the 2010 population census of the people’s republic of china. http://www.stats.gov.cn/tjsj/pcsj/rkpc/6rp/indexch.htm. Accessed 10 December 2018.

6. Outline for the Development of Children in China (2011-2020). http://www.gov.cn/gongbao/content/2011/content_1927200.htm. Accessed 10 December 2018.

7. Statistical Monitoring Report of “China's Outline for Children's Development (2011-2020)” at 2016. http://www.stats.gov.cn/tjsj/zxfb/201710/t20171026_1546618.html. Accessed 10 December 2018.

8. Yu HJ, Gu JX. Legal reflection on the ICU giving up treatment. Tianjin Legal Science. 2013; 113: 70-5.
9. Turner-Stokes L. A matter of life and death: controversy at the interface between clinical and legal decision-making in prolonged disorders of consciousness. J Med Ethics. 2017;43:469-75.

10. Yu HJ, Gu JX. Ethical reflection on the abandon treatment of the ICU. Chinese Medical Ethics, 2012, 25:795-6.

11. Davis, AJ. Book Review: And a time to die: how American hospitals shape the end of life. Nursing Ethics. 2006;13(1):96-7.

12. Luce JM, White DB. The Pressure to Withhold or Withdraw Life-Sustaining Therapy From Critically Ill Patients in the United States. American Journal of Respiratory & Critical Care Medicine. 2007;175(11):1104-8.

13. Ntantana A, Matamis D, Savvidou S, Marmanidou K, Giannakou M, Gouva M, et al. The impact of healthcare professionals' personality and religious beliefs on the decisions to forego life sustaining treatments: an observational, multicentre, cross-sectional study in Greek intensive care units. BMJ Open. 2017;7(7):e013916.

14. Bandrauk N, Downar J, Paunovic B. Withholding and withdrawing life-sustaining treatment: The Canadian Critical Care Society position paper. Canadian Journal of Anaesthesia. 2017; 65(Suppl):105-22.

15. Council AR, Council NZR. Management after Resuscitation in Paediatric Advanced Life Support. ARC and NZRC Guideline 2010. Emergency Medicine Australasia. 2011; 23(4):417-8.

16. Jensen, Hanne, Ammentorp, et al. Guideline for Withholding and Withdrawing Therapy At the Icu: Can It Improve Interdisciplinary Collaboration and Patient Care? Critical Care Medicine. 2011;39.

17. David Häské, Stuke L, Bernhard M, et al. Comparison of the Pre-hospital Trauma Life Support (PHTLS) Recommendations and the German National Guideline on Treatment
of Patients with Severe and Multiple Injuries. Journal of Trauma and Acute Care Surgery. 2016; 81(2):1.

18. Schneider K, Metze B, Bührer C, Cuttini M, Garten L. End-of-Life Decisions 20 Years after EURONIC: Neonatologists’ Self-Reported Practices, Attitudes, and Treatment Choices in Germany, Switzerland, and Austria. J Pediatr. 2019;207:154-60.

19. Kim MJ, Lee JH, Lee HD. Recent Changes in End-of-Life Decisions for Newborns in a Korean Hospital. Am J Hosp Palliat Care. 2018;35(4):574-8.

20. Von Dessauer B, Benavente C, Monje E, Bongain J, Ordenes N. Limitation of Vital Support in a Chilean Pediatric Intensive Care Unit: 2004-2014. Rev Chil Pediatr. 2017;88(6):751-8.

21. Shi WX, Wang N. Treatment abandonment: the economic impact on ICU strategy. Medicine and philosophy. 2000; 21: 14-5.

22. Li HB, Gu JM, Yang DB, Ding Y, Advances in infant mortality reduction patterns in china. Chinese Journal of Child Health Care. 2012;20:722-4.

23. Zhou J, Qian C, Zhao M, Yu X, Kang Y, Ma X, et al. Epidemiology and outcome of severe sepsis and septic shock in intensive care units in mainland China. PLoS One. 2014;16;9(9):e107181.

24. Morton KE, Richardson A, Coombs MA, Darlington AE. Transferring critically ill babies and children home to die from intensive care. Nurs Crit Care. 2019. doi: 10.1111/nicc.12410.

Figures
Figure 1

Incidence and proportion of withdrawing treatment in 680 children during 2006–2017.
Figure 2

The median age of children whose treatment was withdrawn during 2006-2017.