Academic Journal of Medicine & Health Sciences
ISSN 2616-5791 Vol. 7, Issue 1: 87-94, DOI: 10.25236/AJMHS.2026.070113

From the Perspective of Medical Staff: Attitudes toward Pain and End-of-Life Issues in Children with Locked-in Syndrome

Chunyan Yang[1,2], Jianan Xie[1,2], Meiqi Li[3], Wangshan Huang[1], Steven Laureys[3,4], Haibo Di[1,*]

[1]International Vegetative State and Consciousness Science Institute, Hangzhou Normal University, Hangzhou, China
[2]School of Nursing, Hangzhou Normal University, Hangzhou, China
[3]Hangzhou First People's Hospital, Hangzhou, China
[4]Joint International Research Unit on Consciousness, CERVO Brain Research Centre, Laval University, Quebec, Canada
**Corresponding author*

***Abstract:** Locked-in syndrome (LIS), caused by brainstem lesions or severe neurological disorders, is characterized by preserved consciousness and cognition despite complete loss of motor function. In the context of pain management and end-of-life decision-making for pediatric LIS patients, healthcare professionals face ethical challenges shaped by divergent viewpoints. This study examines whether professional medical background influences such perspectives. We surveyed healthcare professionals across six provinces and municipalities in China between July 2023 and November 2024 to investigate their attitudes toward the ethics of life-sustaining treatment in LIS, yielding 628 valid responses. Chi-square tests and binary logistic regression were used for statistical analysis. The mean age of respondents was 33 years; most were young adults (44.4%) and female (64.5%). Professional composition included nurses (26.8%), neurologists or neuroscience researchers (21.4%), other clinicians (19.8%), rehabilitation therapists (15.2%), other staff (14.2%), and medical students (1.7%). Most respondents (87.3%) agreed that children with LIS can perceive pain. Binary logistic regression revealed that the number of children respondents had was significantly associated with their judgment of pain perception in pediatric LIS. Regarding the withdrawal of life-sustaining treatment, 73.6% of respondents expressed negative attitudes. Regression analysis showed that monthly income was significantly associated with attitudes toward treatment withdrawal. Chi-square tests revealed a significant association between pain perception and approval of treatment withdrawal from a third-person perspective ($\chi^2 = 7.152$, $p = 0.007$), whereas no such association was observed from a first-person perspective. Further regression models demonstrated that monthly income, professional role, and number of children were significantly associated with the willingness to sustain life-support treatment. Healthcare professionals' views on pain perception and life-sustaining treatment for pediatric LIS are influenced by their personal characteristics. These attitudinal differences reflect both ethical values and clinical judgments regarding the subjective experience of pediatric patients. Ethical decision-making therefore requires comprehensive and multi-stakeholder deliberation.*

***Keywords:** Locked-in Syndrome; Children; Pain; Life-sustaining treatment; Ethics*

1. Introduction

With advances in critical care medicine, an increasing number of patients with severe brain injury survive with the intervention of life-sustaining treatment (LST). Locked-in Syndrome (LIS) is one such condition requiring LST, typically caused by brainstem injury or other severe neurological disorders. LIS is often confounded with disorders of consciousness (DoC), with a misdiagnosis rate as high as 40%, potentially leading to inappropriate medical decisions, particularly in patients with recovery potential[1-7]. The primary characteristic of patients with LIS is generalized motor paralysis with complete preservation of consciousness and typically intact cognitive function[3]. Based on residual motor function, LIS can be classified into three types: classic (only eye blinking preserved), incomplete (some voluntary limb movements preserved), and complete (consciousness detectable only by electroencephalography)[8].

The overall prevalence of LIS in the general population remains unclear and varies by region. For pediatric patients living with LIS, pain assessment and management represent one of the primary challenges they face. Unlike other patients, these children are unable to effectively communicate their pain through verbal or physical expression; moreover, due to the immaturity of their developing nervous systems, their pain expression patterns differ significantly from those of adults[9, 10]. In the absence of established communication methods, healthcare professionals often must rely on indirect assessment approaches to determine the presence and extent of pain[11, 12]. The treatment and care of children with LIS involve complex physical, emotional, and psychological challenges, necessitating comprehensive support and care.

Although the clinical features and pathophysiological mechanisms of LIS have been relatively well established, much remains unknown regarding its long-term prognosis and management strategies[12]. Among various clinical decisions, whether to continue LST has emerged as a central ethical issue[13, 14] . Particularly for pediatric LIS patients with recovery potential, research indicates that their prognosis is generally better than that of adults, a finding crucial for care planning and end-of-life decision-making[14]. Such decisions typically rely on surrogate decision-makers (primarily parents and the medical team), requiring healthcare professionals to balance medical indications, ethical dilemmas, legal responsibilities, and the emotional needs of families to ensure a comprehensive and humane decision-making process.In this process, third-party attitudes play a significant heuristic role in decision-making.[15] . How to balance medical interventions with the best interests of the child, while respecting family wishes, constitutes a complex ethical issue in the medical management of children with LIS.

Given that ethical research on patients with LIS has predominantly focused on adults, studies in the pediatric population remain relatively scarce[14-17]. Therefore, gaining an in-depth understanding of healthcare professionals' attitudes toward pain perception and end-of-life decision-making in children with Locked-in Syndrome is particularly important.

2. Methods

This study was approved by the Ethics Committee of Hangzhou Normal University (Ethics Approval Number: 2025016). A voluntary and anonymous questionnaire survey was conducted, with completion of the questionnaire by participants considered as informed consent and voluntary participation. A total of 628 questionnaires were collected from six provinces and municipalities (Beijing, Shanghai, Zhejiang Province, Hunan Province, Guangdong Province, and Shaanxi Province) between July 2023 and November 2024. At the beginning of the questionnaire, we described the typical characteristics of children with LIS and those with other disorders of consciousness to help respondents effectively distinguish between categories, after which they answered yes/no questions related to LIS[17]. Demographic data were collected, including gender, age, and specific occupation. This study reported healthcare professionals' responses to the following questions: "Do you think children with LIS can feel pain?" (Yes/No); "Do you agree with withdrawing life support systems from children with LIS?" (Agree/Disagree); "If your child were in a state of LIS, would you be willing to continue life-sustaining treatment?" (Willing/Unwilling). To ensure comparability with European surveys, six items also included attitudinal questions regarding UWS and MCS. Finally, based on early literature published in Europe in 2014 and its Chinese adaptation for adults by the research team in 2019[5], the questionnaire was adjusted for pediatric populations in 2022, optimized based on expert review, pre-testing, and suggestions in the field of DoC, and formally published after reaching consensus.

3. Statistical Analysis

Data analysis was performed using SPSS software (version 25.0). Frequencies and percentages were used for descriptive statistics. Chi-square tests and logistic regression analyses were conducted to explore the influence of various factors on healthcare professionals' attitudes. Chi-square tests were used to assess differences within and between categorical variables. Binary logistic regression was employed to examine factors associated with consistency in responses, estimating odds ratios (OR) and 95% confidence intervals (CI). Statistical significance was set at $p < 0.05$ (two-tailed).

4. Results

4.1 Demographic Characteristics of Respondents

Among the 628 respondents, the mean age was 33.18 ± 8.396 years, with the majority aged 20-30 years (44.4%). Females predominated, accounting for 64.5% of the sample. Regarding professional backgrounds, nurses constituted the largest group (26.8%), followed by neurologists/neuroscience researchers (21.4%), other clinical physicians (19.8%), rehabilitation therapists/technicians (15.2%), other healthcare personnel (14.2%), and medical students (1.7%). The diverse professional backgrounds facilitated understanding of healthcare professionals' perspectives on children with LIS. In this survey, the majority of respondents (93.8%) reported no religious affiliation; among those with religious beliefs, Buddhism was the most prevalent (n=27). A total of 710 questionnaires were distributed, yielding a response rate of approximately 88.73% and an exclusion rate of approximately 11.53%. Detailed information is presented in Table 1.

Table 1. Demographic Characteristics of Respondents (N=628)

	Stratification	Frequency(n)	Percentage(%)
Age	20-30 years	280	44.4
	31-40 years	245	38.8
	41-50 years	74	11.7
	>50 years	29	4.6
Gender	Male	223	35.3
	Female	405	64.5
Religious Belief	Buddhism	27	4.3
	Christianity	3	0.5
	Islam	2	0.3
	Other	4	0.6
	NO	592	93.8
Monthly Income	≤2,000	61	9.7
	2,001-5,000	70	11.1
	5,001-10,000	282	44.7
	10,001-20,000	177	28.1
	>20,000	38	6.0
Education Level	Bachelor's Degree or Below	357	56.8
	Master's Degree or Above	271	43.2
Professional Category	Neurologists/Neuroscience Researchers	135	21.4
	Other Clinical Physicians	125	19.8
	Nursing Staff	125	26.8
	Rehabilitation Therapists/Technicians	169	15.2
	Other Healthcare Personnel	92	14.2
	Medical Students*	11	1.7
Parental Status (Having/raising children)	Yes	334	52.2
	No	294	46.8

*Healthcare Professionals Including Medical Students (Resident Physicians, Student Nurses)

4.2 Attitudes Toward Pain Perception and Life-Sustaining Treatment in Children with LIS

Overall, the vast majority of respondents (87.3%) agreed that patients with LIS can perceive pain (Table 2). Logistic regression analysis revealed (Table 3) that profession and number of children were significant factors influencing this perception. More specifically, nursing staff and healthcare professionals with one child were more likely to acknowledge that children with LIS can feel pain. Among those who denied pain perception (12.7%), the majority were nurses (n=32, 18.9%), followed by neurologists (n=9, 6.7%) and other clinical physicians (n=15, 12.0%). A greater proportion of respondents (56.4%) considered that prolonged LIS in children is worse than VS or MCS; however, this view was not held when considering the perspective of the children's families (Table 2).

Table 2. Attitudes Toward Pain Perception and Life-Sustaining Treatment in Children with LIS

Item	Response	Frequency	Percentage
Do you think children with Locked-in Syndrome can feel pain?	Yes	548	87.3%
	No	80	12.7%
Do you think that for pediatric patients, prolonged Locked-in Syndrome is worse than being in a chronic vegetative state or chronic minimally conscious state?	Yes	354	56.4%
	No	274	43.6%
Do you think that for the families of pediatric patients, prolonged Locked-in Syndrome in their child is worse than the child being in a chronic vegetative state or chronic minimally conscious state?	Yes	285	45.4%
	No	343	54.6%
Do you agree with withdrawing life support systems from children with Locked-in Syndrome?	Agree	166	26.4%
	disagree	462	73.6%
If your child were in a prolonged state of Locked-in Syndrome, would you be willing to continue life-sustaining treatment for him/her?	Willing	527	83.9%
	Unwilling	101	16.1%

Regarding attitudes toward life-sustaining treatment in LIS, the majority of respondents (73.6%) answered negatively to the question of whether to withdraw life-sustaining treatment from children with LIS (Table 2). Logistic regression analysis showed (Table 3) that monthly income and education level were significantly associated with attitudes toward withdrawal of life-sustaining treatment. Studies have indicated that when end-of-life issues pertain to oneself, there exists a divergence between general preferences and personal preferences [19]. Consistent with this finding, when respondents imagined their own child being in a prolonged state of LIS, more participants (83.9%) expressed willingness to continue life-sustaining treatment for their child (Table 2). Logistic regression analysis revealed (Table 3) that monthly income, being a rehabilitation therapist/technician, and number of children were significantly associated with willingness to continue life-sustaining treatment. Detailed information is presented in Table 3.

Table 3. Logistic Regression Analysis of Factors Predicting Consistency in Questionnaire Responses Among Chinese Healthcare Professionals Regarding Children with LIS

Item	Predictor Do you think patients with Locked-in Syndrome can feel pain? OR(95%CI)	Do you agree with withdrawing life support systems from children with Locked-in Syndrome?OR (95% CI)	If your child were in a prolonged state of Locked-in Syndrome, would you be willing to continue life-sustaining treatment for him/her?OR (95% CI)
1		Reference category: first	
2	0.613(0.184-2.042)	2.201(0.899-5.392)	0.485(0.166-1.413)
3	0.5(0.173-1.443)	1.269(0.563-2.861)	0.628(0.24-1.643)
4	0.369(0.123-1.105)	2.232(0.977-5.102)	0.342(0.13-0.903)*
5	0.383(0.088-1.668)	3.447(1.24-9.587)*	0.466(0.131-1.666)
a	0.974(0.539-1.757)	0.582(0.374-0.907)*	1.31(0.782-2.196)
A			
B	0.599(0.249-1.438)	1.229(0.692-2.183)	1.648(0.862-3.151)
C	0.336(0.14-0.807)*	1.35(0.743-2.453)	1.824(0.916-3.631)
D	0.85(0.305-2.371)	0.626(0.312-1.253)	3.715(1.549-8.911) *
E	0.395(0.159-0.979)*	1.419(0.765-2.634)	1.295(0.647-2.595)
F	0.294(0.05-1.721)	0.999(0-0)	476823475.5(0)
A1	* Reference category: first		* Reference category: first
B2	2.347(1.209-4.556)*	0.862(0.549-1.353)	1.921(1.119-3.298) *
C3	1.015(0.552-1.868)	0.737(0.442-1.231)	2.335(1.222-4.464) *

Note: Monthly income below-2000:1; 2-5 thousand: 2; 5 thousand-10,000:3; 10,000-20,000:4; above 20,000:5; Education level-university or below: a. Specific occupation: Neurologist/neurology researcher: A; Other clinical doctors: B; Nursing: C; Rehabilitation therapist/technician: D; Other medical personnel: E; Medical student: F Number of children: one=A1;two=B2; above2=C3

4.3 Influence of Perspective Differences on Decision-Making

The relationship between pain perception and the decision to withdraw life support systems in patients with Locked-in Syndrome (LIS) was examined from different perspectives (first-person vs. third-person), as shown in Table 4. Chi-square test results revealed that the association between pain perception and withdrawal of life support systems was statistically significant in the third-person perspective (χ^2=7.152, p=0.007), indicating that the presence or absence of pain perception significantly influenced decision-making in this perspective. Conversely, this relationship was not significant in the first-person perspective.

Table 4. Relationship Between Pain Perception and LST Decision-Making from Different Perspectives

Perspective	Withdrawal		No Withdrawal	x^2	p
Third-Person Perspective (LIS)	Pain Perceived	135(24.6%)	413(75.4%)	7.152	0.007
	No Pain Perceived	31(38.8%)	49(61.3%)		
First-Person Perspective (LIS)	Pain Perceived	462(87.7%)	86(85.1)	0.483	0.487
	No Pain Perceived	65(12.3%)	15(14.9%)		

Note: Third-Person Perspective - "Do you agree with withdrawing life support systems from children with Locked-in Syndrome?" First-Person Perspective - "If your child were in a prolonged state of Locked-in Syndrome, would you be willing to continue life-sustaining treatment for him/her?"

5. Discussion

This study, through a large-sample survey of 628 healthcare professionals, systematically examined their ethical attitudes toward pain perception and life-sustaining treatment (LST) in children with Locked-in Syndrome (LIS) and the factors influencing these attitudes. The findings revealed that although the vast majority of healthcare professionals acknowledged the pain perception capacity of children with LIS and, in principle, opposed the withdrawal of LST, their attitudes were significantly influenced by personal characteristics (such as profession, income, and number of children) and decision-making perspective (first-person vs. third-person), revealing the complexity of this ethical issue.

First, 87.3% of respondents in this study acknowledged that children with LIS can feel pain, which is highly consistent with previous research findings on patients with LIS both domestically and internationally [5, 12, 18, 19]. It is worth noting that nursing staff, due to their more frequent and closer contact with patients' daily lives, may pay greater attention to children's non-verbal expressions and subtle reactions, thereby more readily identifying pain signals in children with LIS. Moreover, the rarity of LIS often contributes to unclear understanding[6]. This study also found that healthcare professionals with children were more likely to acknowledge pain perception in children with LIS, possibly stemming from their daily experience in child-rearing, thus enabling them to more acutely identify pain signals in pediatric patients. When comparing disorders of consciousness with LIS, a greater proportion of respondents (56.4%) considered prolonged LIS in children to be worse than VS or MCS; however, this view was not held when considering the perspective of the children's families, which is consistent with the findings of Demertzi et al., though the opposite pattern was observed for patients with VS[5, 20]. Interestingly, within the same medical profession, other healthcare personnel and nursing staff were more likely than neurologists to believe that children with LIS can feel pain. This may be attributable to the questionnaire's lack of explanation regarding the concept of pain, leading to differences in understanding [22].

Although existing literature does not directly compare pain perception differences between children and adults with LIS, based on the high sensitivity of the pediatric nervous system and the complexity of pain assessment, it is hypothesized that children with LIS may experience more intense pain than adults[21, 22]. Although children with LIS have limited mobility, their consciousness remains intact, enabling them to communicate through eye contact or assistive devices, which provides opportunities for interaction with family members, offers some comfort, and alleviates family suffering. In contrast, the "absence" experienced by families of children in a vegetative state (VS) often leads to feelings of loneliness and helplessness. Additionally, while caring for affected children, family members may lose normal social engagement and earning capacity, further exacerbating their psychological and economic burden[23, 24]. Given the unique living condition of children with LIS, patients, families, and society may hold different perspectives regarding whether to continue life-sustaining treatment. All parties require comprehensive communication and negotiation to make decisions that align with the patient's best interests [19, 25, 26].

Here, we found that healthcare professionals with higher monthly income were more likely to support withdrawal of life-sustaining treatment in children with LIS. This finding contrasts with previous research on cancer survival rates in children, which demonstrated lower survival rates in low-income regions compared to high-income areas[27, 28]. This discrepancy may be related to higher-income healthcare professionals' comprehensive considerations regarding ethical deliberation, psychological and emotional responses, and medical resource allocation[25]. Such differences exist not only between regions but also between countries; physicians in high-income countries and regions may be more inclined to prevent unnecessary suffering by withholding or withdrawing life-sustaining treatment, whereas those in low- and middle-income countries and regions tend to focus more on the legal risks associated with life-sustaining treatment and express greater desire for relevant legislation. For example, impoverished families in the United States face substantial income loss risks due to childhood cancer treatment, and financial burden can potentially push even previously non-impoverished families into poverty[29]. Similar situations exist in Asia, where respondents from low- and middle-income countries and regions showed independently and significantly lower likelihood of refusing life-sustaining treatment compared to those from high-income countries and regions [31].

Perspectives on life-sustaining treatment for patients with LIS vary across countries. A European survey found that 90% of respondents believed patients with LIS can perceive pain, and 75% opposed treatment discontinuation. However, when imagining themselves in a similar situation, 56% expressed a desire not to continue living, indicating that individuals tend to prefer ending life rather than sustaining it when personally facing life-sustaining treatment decisions, consistent with previous research findings[27]. German neurologists are less likely to limit life-sustaining treatment in patients with LIS, which may be attributable not only to differing categorical descriptions of life-sustaining treatment in research but also to the finding that the presence or absence of consciousness does not appear to be the basis for neurologists' decisions to limit life-sustaining treatment. This aligns with findings from a Chinese study suggesting that life-sustaining treatment should not be withdrawn from patients with chronic LIS, as these patients can clearly experience the world and their condition is neither terminal nor irreversible[17, 23]. The American Academy of Neurology has also emphasized the importance of respecting autonomy and improving quality of life for patients with LIS[30, 31]. All patients possess human rights, including the right to consent to or refuse treatment[32]. However, China currently lacks clear legal provisions supporting life-sustaining treatment, rendering this area highly controversial domestically. Different countries have distinct cultural and legal systems; South Korea implemented legislation regarding life-sustaining treatment decisions in February 2018, applicable to patients who are terminally ill, have incurable conditions, or are in a persistent vegetative state, respecting patient autonomy and protecting their best interests[33]. Norwegian law stipulates that the healthcare system cannot refuse treatment if it aligns with the child's best interests[34]. In conclusion, decisions regarding life-sustaining treatment are influenced more by local legislation than by individual attitudes, and future research should consider both ethical and legal perspectives.

However, nearly one-quarter of healthcare professionals believed that life-sustaining treatment could be withdrawn from children with LIS, a finding that exceeded our initial hypothesis. Nevertheless, this is relatively consistent with the proportion observed in Chinese scholars' surveys regarding withdrawal of life-sustaining treatment in adults with LIS[16]. Although children with LIS retain consciousness, preserving life does not always represent their best interests; under specific circumstances where treatment cessation aligns with the child's best interests and may potentially result in death, treatment may be withheld or withdrawn, while also considering the overall interests of the family[35, 36]. Due to the difficulty in accurately predicting future quality of life and determining what constitutes a life worth living, establishing a clear "baseline" proves extremely challenging. Research indicates that in the most severe cases, most people consider life not worth living for a severely disabled infant, with up to 50% of participants believing life-sustaining treatment could be withdrawn [31]. Interestingly, when healthcare professionals faced the scenario of their own child being in a state of LIS, the proportion willing to forgo life-sustaining treatment decreased significantly (16.1%). This differs from previous research, suggesting that decision-making for oneself versus others may vary due to differing positions and roles[16].

Although the ethical foundation for decision-making in adults derives from the principle of informed consent, many children lack the full capacity to provide consent, necessitating respect for their developmental autonomy while also supporting the needs of the entire family[37]. When children face acute situations, the medical decisions made by physicians may sometimes lead to serious ethical dilemmas, with legal issues subsequently arising[38]. In many cultures, particularly Asian cultures, life is regarded as sacred and inviolable, especially regarding children's lives, and decisions to forgo treatment are typically not made lightly[17, 39].This study found that most respondents provided consistent answers to questions regarding life-sustaining treatment in LIS from both third-person and first-person perspectives, generally opposing the termination of life in LIS, which aligns with previous research findings in adults[16]. Healthcare professionals in the third-person perspective focused more on whether the child was suffering, paying greater attention to overt manifestations of suffering (such as pain) and being more readily driven by moral responsibility. In contrast, from the first-person perspective, they were more inclined to relieve their own child from distress, placing greater emphasis on quality of life and subjective experience, with pain perception exerting weaker influence. Medical decisions vary according to differences in perspective[35]. Therefore, the primacy of patients' subjective wishes is paramount, rather than judgments based solely on observers' perspectives[32]. In the management of patients with LIS, greater emphasis should be placed on patients' subjective wishes and pain perception, while comprehensively considering family members' emotional needs and quality of life, to achieve more comprehensive and humane medical decision-making.

6. Conclusion

Healthcare professionals' attitudes toward pain perception and LST decisions in children with disorders of consciousness are shaped by demographic factors. Perspectives on LST withdrawal differ notably in third-person contexts, reflecting diverse views on life value, parent-child bonds, and pain awareness. These findings highlight the need for individualized care and ethical sensitivity in pediatric practice. Enhancing ethics training and pain-related education is essential to support more informed and compassionate LST decision-making.

Acknowledgement

This study was supported by the National Natural Science Foundation of China (Grant No. 81920108023) under the project “Research on the correlation of posterior cortical consciousness based on clinical evidence of disorders of consciousness”.

References

[1] SCHNAKERS C. Assessing consciousness and cognition in disorders of consciousness [J]. NeuroRehabilitation, 2024, 54(1): 11-21.
[2] CORTESE M D, RIGANELLO F, ARCURI F, et al. Coma recovery scale-r: variability in the disorder of consciousness [J]. BMC Neurol, 2015, 15: 186.
[3] DAS J M, ANOSIKE K, ASUNCION R M D. Locked-in Syndrome [M]. StatPearls. Treasure Island (FL); StatPearls Publishing
Copyright © 2025, StatPearls Publishing LLC. 2025.
[4] BAUER G, GERSTENBRAND F, RUMPL E. Varieties of the locked-in syndrome [J]. J Neurol, 1979, 221(2): 77-91.
[5] KOHNEN R F, LAVRIJSEN J C, BOR J H, et al. The prevalence and characteristics of patients with classic locked-in syndrome in Dutch nursing homes [J]. J Neurol, 2013, 260(6): 1527-1534.
[6] WHYTE J, POULSEN I, NI P, et al. Development of a Measure of Nociception for Patients With Severe Brain Injury [J]. Clin J Pain, 2020, 36(4): 281-288.
[7] HUMMEL P, VAN DIJK M. Pain assessment: current status and challenges [J]. Semin Fetal Neonatal Med, 2006, 11(4): 237-245.
[8] VITELLO M M, SZYMKOWICZ E, LAUREYS S, et al. Neuroimaging and neurophysiological diagnosis and prognosis in paediatric disorders of consciousness [J]. Dev Med Child Neurol, 2022, 64(6): 681-690.
[9] BONIN E A C, LEJEUNE N, SZYMKOWICZ E, et al. Assessment and management of pain/nociception in patients with disorders of consciousness or locked-in syndrome: A narrative review [J]. Front Syst Neurosci, 2023, 17: 1112206.
[10] HALAN T, ORTIZ J F, REDDY D, et al. Locked-In Syndrome: A Systematic Review of Long-Term Management and Prognosis [J]. Cureus, 2021, 13(7): e16727.
[11] BERNAT J L. Medical Decision Making by Patients in the Locked-in Syndrome [J]. Neuroethics, 2018, 13(2): 229-238.
[12] BRUNO M A, SCHNAKERS C, DAMAS F, et al. Locked-in syndrome in children: report of five cases and review of the literature [J]. Pediatr Neurol, 2009, 41(4): 237-246.
[13] YAN Y, DEMERTZI A, XIA Y, et al. Ethics of life-sustaining treatment in locked-in syndrome: A Chinese survey [J]. Ann Phys Rehabil Med, 2020, 63(6): 483-487.
[14] KUEHLMEYER K, RACINE E, PALMOUR N, et al. Diagnostic and ethical challenges in disorders of consciousness and locked-in syndrome: a survey of German neurologists [J]. J Neurol, 2012, 259(10): 2076-2089.
[15] DEMERTZI A, JOX R J, RACINE E, et al. A European survey on attitudes towards pain and end-of-life issues in locked-in syndrome [J]. Brain Inj, 2014, 28(9): 1209-1215.
[16] LI M, YAN Y, KUEHLMEYER K, et al. Clinical and ethical challenges in decision-making for

patients with disorders of consciousness and locked-in syndrome from Chinese neurologists' perspectives [J]. Ther Adv Neurol Disord, 2024, 17: 17562864241283328.

[17] EDLOW B L, CLAASSEN J, SCHIFF N D, et al. Recovery from disorders of consciousness: mechanisms, prognosis and emerging therapies [J]. Nat Rev Neurol, 2021, 17(3): 135-156.

[18] TONG H, MALONEY T C, PAYNE M F, et al. Processing of pain by the developing brain: evidence of differences between adolescent and adult females [J]. Pain, 2022, 163(9): 1777-1789.

[19] DUFF I T, KROLICK K N, MAHMOUD H M, et al. Current Evidence for Biological Biomarkers and Mechanisms Underlying Acute to Chronic Pain Transition across the Pediatric Age Spectrum [J]. J Clin Med, 2023, 12(16).

[20] RAJA S N, CARR D B, COHEN M, et al. The revised International Association for the Study of Pain definition of pain: concepts, challenges, and compromises [J]. Pain, 2020, 161(9): 1976-1982.

[21] RACITI L, CORALLO F, MANULI A, et al. Nursing, Caregiving and Psychological support in Chronic Disorders of Consciousness: a scoping review [J]. Acta Biomed, 2021, 92(S2): e2021013.

[22] YOSHIKI H, MORIMOTO N, URAYAMA K Y. Understanding the Psychological Well-being of Patients With Locked-in Syndrome: A Scoping Review [J]. Cureus, 2023, 15(1): e34295.

[23] LEO A, NARO A, CANNAVò A, et al. Could autonomic system assessment be helpful in disorders of consciousness diagnosis? A neurophysiological study [J]. Exp Brain Res, 2016, 234(8): 2189-2199.

[24] RITTER J, ALLEN S, COHEN P D, et al. Financial hardship in families of children or adolescents with cancer: a systematic literature review [J]. Lancet Oncol, 2023, 24(9): e364-e375.

[25] EHRLICH B S, MCNEIL M J, PHAM L T D, et al. Treatment-related mortality in children with cancer in low-income and middle-income countries: a systematic review and meta-analysis [J]. Lancet Oncol, 2023, 24(9): 967-977.

[26] PHUA J, JOYNT G M, NISHIMURA M, et al. Withholding and withdrawal of life-sustaining treatments in low-middle-income versus high-income Asian countries and regions [J]. Intensive Care Med, 2016, 42(7): 1118-1127.

[27] LAUREYS S, PELLAS F, VAN EECKHOUT P, et al. The locked-in syndrome : what is it like to be conscious but paralyzed and voiceless? [J]. Prog Brain Res, 2005, 150: 495-511.

[28] Position statement: certain aspects of the care and management of profoundly and irreversibly paralyzed patients with retained consciousness and cognition. Report of the Ethics and Humanities Subcommittee of the American Academy of Neurology [J]. Neurology, 1993, 43(1): 222-223.

[29] BONA K, DUSSEL V, ORELLANA L, et al. Economic impact of advanced pediatric cancer on families [J]. J Pain Symptom Manage, 2014, 47(3): 594-603.

[30] LARCHER V, CRAIG F, BHOGAL K, et al. Making decisions to limit treatment in life-limiting and life-threatening conditions in children: a framework for practice [J]. Arch Dis Child, 2015, 100 Suppl 2: s3-23.

[31] WOSINSKI B, NEWMAN C J. Physicians' attitudes when faced with life-threatening events in children with severe neurological disabilities [J]. Dev Neurorehabil, 2019, 22(1): 61-66.

[32] DEMERTZI A, RACINE E, BRUNO M A, et al. Pain Perception in Disorders of Consciousness: Neuroscience, Clinical Care, and Ethics in Dialogue [J]. Neuroethics, 2012, 6(1): 37-50.

[33] VARKEY B. Principles of Clinical Ethics and Their Application to Practice [J]. Med Princ Pract, 2021, 30(1): 17-28.

[34] HEO D S, YOO S H, KEAM B, et al. Problems Related to the Act on Decisions on Life-Sustaining Treatment and Directions for Improvement [J]. J Hosp Palliat Care, 2022, 25(1): 1-11.

[35] TANAKA GUTIEZ M, EFSTATHIOU N, INNES R, et al. End-of-life care in the intensive care unit [J]. Anaesthesia, 2023, 78(5): 636-643.

[36] NIZZI M, BLANDIN, V. & DEMERTZI, A. . Attitudes towards Personhood in the Locked-in Syndrome: from Third- to First- Person Perspective and to Interpersonal Significance. [J]. Neuroethics 2020.

[37] KIRSCH R E, BALIT C R, CARNEVALE F A, et al. Ethical, Cultural, Social, and Individual Considerations Prior to Transition to Limitation or Withdrawal of Life-Sustaining Therapies [J]. Pediatr Crit Care Med, 2018, 19(8S Suppl 2): S10-s18.

[38] SISK B A, DUBOIS J, KODISH E, et al. Navigating Decisional Discord: The Pediatrician's Role When Child and Parents Disagree [J]. Pediatrics, 2017, 139(6).

[39] MERLO F, MALACRIDA R, HURST S, et al. Physicians' decision-making when managing pediatric patients with prolonged disorders of consciousness: A qualitative study [J]. Eur J Neurol, 2022, 29(8): 2181-2191.