Gross Motor Developmental Function Outcomes in Infantile and Toddler Pediatric Intensive Care Unit Survivors

Chun-Feng Yang
Jilin University First Hospital
Yang Xue
Jilin University First Hospital
Jun-Yan Feng
Jilin University First Hospital
Fei-Yong Jia
Jilin University First Hospital
Yu Zhang
Jilin University First Hospital
Yu-Mei Li (liyumei1989@126.com)

Research article

Keywords: Gross Motor Developmental Function, Sepsis, Mechanical Ventilation, Pediatric Intensive Care Unit, Infant, Toddler

Posted Date: September 27th, 2019

DOI: https://doi.org/10.21203/rs.2.15247/v1

Version of Record: A version of this preprint was published on December 21st, 2019. See the published version at https://doi.org/10.1186/s12887-019-1893-9.

Abstract

Background In recent years, increasing studies have focused on motor function/dysfunction in PICU survival. However, most studies have focused on adults and older children. This study aims to investigate gross motor developmental function outcomes in infantile and toddler pediatric intensive care unit (PICU) survivors and the factors associated with gross motor developmental functions.

Methods Thirty-five eligibles were divided into dysfunctional (n=24) or non-dysfunctional (n=11) group. Baseline gross motor function for all participants before PICU admission was measured via the Age and Stages Questionnaires, Third Edition (ASQ-3). The Peabody Developmental Motor Scales, Second Edition (PDMS-2) was used to evaluate gross motor development function before PICU discharge.

Results The gross motor developmental dysfunction incidence was 68.6% in this study. Linear correlation analysis showed that the GMQ was positively correlated with pediatric critical illness score (PCIS, r=0.621, P<0.001), and negatively correlated with length of PICU stay (r=-0.556, P=0.001), days sedated (r=-0.602, P<0.001), days on invasive mechanical ventilation (IMV; r=-0.686, P<0.001), and days on continuous renal replacement therapy (CRRT; r=-0.538, P=0.001). Linear regression analysis showed that IMV days (β=-0.736, P=0.001), sepsis (β=-18.111, P=0.003) and PCIS (β=0.550, P=0.021) were independent risk factors for gross motor developmental dysfunction

Conclusions Gross motor developmental dysfunction in infantile and toddler PICU survivors are more common and may be exacerbated by experiences associated with longer IMV days and increasing illness severity combined with sepsis.

Introduction

In recent years, with improved diagnostic and treatment technology in pediatric critical care medicine, the mortality rate among critically ill children has decreased significantly. However, treatments such as invasive mechanical ventilation (IMV), drugs and other factors, can also cause newly acquired functional disabilities, in addition to saving the lives of critically ill children[1–3]. In recent years, increasing studies have focused on motor function/dysfunction in PICU survival[1, 4, 5]. However, most studies have focused on adults and older children. Because motor function in older children is similar to that in adults, the methods mostly assess muscle strength, mobility, fatigue and the activities of daily living scale (ADLS), and most assessment results are obtained via questionnaires[4, 6–8]. However, these assessment methods do not apply to infants and toddlers in the PICU. Because children are not “little adults”[9], their gross motor functions are in the developmental stage, which is a critical period for gaining motor skills. Therefore, assessing gross motor developmental function can better reflect the physical functions of children in this age group.

Few studies have focused on acquired gross motor developmental dysfunction in children. Hövels-Gürich HHet al.[10] found that the neonatal arterial switch operation with combined circulatory arrest and low-

flow bypass was associated with neurological and fine and gross motor impairment. In addition, gross motor developmental function assessment was mostly used in neonatal intensive care units (NICUs) and in high-risk infants[11, 12]. Most of these patients have congenital gross motor developmental dysfunction, while PICU patients have mostly acquired gross motor developmental dysfunction, and the two populations differ entirely[13, 14]. Therefore, our study investigated the gross motor developmental function outcomes of infantile and toddler survivors of pediatric intensive care units (PICUs) and is the first to assess gross motor developmental function in infants and toddlers in a PICU.

Methods

Patients

This observational study was conducted in the pediatric intensive care unit of the First Hospital of Jilin University, ChangChun, China. Eligible cases were children aged between 1 month and 3 years who were hospitalized in the PICU ≥ 48h between January 2019 and March 2019, and for whom it was their first PICU admission during the study period. Children were excluded if they had neuromuscular junction disease, central nervous system disease, limb fractures or deep vein thrombosis. Children with gross motor developmental dysfunction before PICU admission were also excluded. The hospital's ethics committee granted permission for the study, and the eligible children's parents/guardians provided written informed consent. The trial was registered at clinical trials.gov (ChiCTR1800020196). All participants' information sheets were provided to their parents.

Procedure

The PICU cohort was categorized into two groups: the dysfunctional group (GMQ<90) or the non-dysfunctional group (GMQ ≥ 90). Age, sex, diagnosis, severity of illness, length of PICU stay, days on IMV, days on methylprednisolone days on sedated, days on CRRT, and application of vasoactive drugs were recorded for each group. Because of the sample size, primary diagnoses were broadly categorized as cardiovascular, respiratory, gastrointestinal, or other (genitourinary, hematologic/oncologic, musculoskeletal, endocrinologic, and trauma). Baseline gross motor function was measured for all participants before PICU admission using the Age and Stages Questionnaires, Edition 3 (ASQ–3) to assess the gross motor developmental function of participants prior to PICU admittance. At the time of PICU discharge, all patients completed the Peabody Developmental Motor Scales, Second Edition (PDMS–2), which assesses gross motor development function[15, 16]. To ensure the accuracy of the assessment results, one experienced physiotherapist assessed all participants in a assessment room which meets conditions for motor assessment.

Measures

Illness severity was measured using the pediatric critical illness score (PCIS)[17] developed by the Chinese Medical Association Emergency Department and the Chinese Medical Association Emergency Society Pediatrics Group. The PCIS is currently the most widely used pediatric critical illness scoring method in China, and it can accurately determine the condition and predict the risk of death in children[18].

The ASQ is a reliable, standardized, parent-completed, developmental screening test composed of 21 age-specific questions covering the ages of 1–66 months[19]. The ASQ–3 encompasses five developmental areas: communication, gross motor, fine motor, problem solving and personal-social[20, 21].Three responses are possible per item, depending on whether the child can perform the task: "Yes" (10points), "Sometimes" (5 points) and "Not Yet" (0 points). The total score for each area is obtained by adding the scores of the six items. The assessment results are divided into normal, critical and abnormal based on each area's total score. Patients with critical and abnormal outcomes were excluded.

At time of PICU discharge, the patients' gross motor developmental function was measured using the PDMS–2, which is a norm-referenced tool designed to assess the fine and gross motor skills of children aged between 0 and 71 months. Its normative sample was based on 2003 children in forty-six states of the United States and one Canadian province[22].The PDMS–2 is suitable for assessing various populations of children at a high risk for motor delays. It has a high degree of reliability and validity regarding child development in China[23–25], but few studies have applied the PDMS–2 to children in PICUs. The PDMS–2 is composed of four subtests: reflex, stationary, locomotion, and object manipulation, and each subtest contributes to the gross motor quotient (GMQ) score. The scores are interpreted as very superior (131–165), superior (121–130), above average (110–120), average (90–109), below average (80–89), poor (70–79), or very poor (35–69)[26]. Gross motor developmental dysfunction was defined as GMQ < 90[26].

Statistical Analyses

Data were analyzed using IBM SPSS Statistics for Windows, version 22.0 (IBM Corp, Armonk, NY, USA). Continuous variables are described as the mean±SD or median (interquartile range), depending on whether distribution was normal or non-normal. Categorical variables are described as n(%). Continuous variables were compared using Student's t-test or the Mann-Whitney U test. Categorical variables were compared using the chi-square test or Fisher's exact test depending on sample size. For the correlation analyses, the Spearman method was used to test the relationship between GMQ and PCIS, length of PICU stay, IMV days, days on methylprednisolone, sedated and CRRT days. The relationship among multiple factors was analyzed via multivariate linear regression (stepwise method), and the dependent variable Y was a continuous variable which distribution was normal. For all final comparisons, $P \leq 0.05$ was considered statistically significant.

Results

Sample Characteristics

During the study period, 70 of 105 PICU patients were excluded. Of these 70 patients, 8 had motor developmental delays before entering the PICU, 18 parents refused permission to undergo the motor development assessment, 10 died during PICU hospitalization, 19 had abnormal ASQ–3 results, and 15 cases was discharged within 48 hours of PICU admittance. Finally, 35 patients met the inclusion criteria. Participants were divided into the children with developmental dysfunction group (n = 24) or children without developmental dysfunction group (n = 11) based on whether the GMQ was < 90 (*Fig 1).*.

Age, sex, diagnostic category, percentage of surgical patients, percentage of sepsis, use of vasoactive medications, PCIS, length of PICU stay, IMV days, days on sedatives, days on methylprednisolone and CRRT days were recorded for both groups (*Table 1).* Of all 35 eligible patients, 24 had gross motor developmental dysfunction with incidence of 68.6% (24/35). PCIS in the dysfunctional group was significantly lower than that in the non- dysfunctional group (81.0±89.09 vs 92.18±5.17, *P* = 0.001). Use of vasoactive medications (57.9% vs 8.3%, *P* = 0.006), length of PICU stay (22.50 [range, 14.50–27.75] vs 9.00 [7.00–17.00], *P* = 0.029), days on sedatives (9.0 [7.0–13.0] vs 1.0 [0.3–2.0], *P* = 0.021), and IMV days (7.46±5.34 vs 1.27±2.83, *P* = 0.001) were significantly higher than those parameters in the non-dysfunctional group.

Linear correlation between GMQ and PCIS, length of PICU stay, IMV days, days on sedatives, days on methylprednisolone, and CRRT days

We performed a linear correlation analysis between the GMQ and PCIS, length of stay in the PICU, IMV days, days on sedatives, days on methylprednisolone, and CRRT days. The results showed that GMQ was positively correlated with PCIS (r = 0.621, *P*<0.001), while length of PICU stay (r = −0.556, *P* = 0.001), days sedated (r = −0.602, *P*<0.001), IMV days(r = −0.686, *P*<0.001), and CRRT days(r = −0.538, *P* = 0.001) were negatively correlated with the GMQ (*Figs. 2A–F)*..

Linear regression analysis between GMQ and length of PICU stay, days on sedatives, IMV days, CRRT days, PCIS, use of vasoactive medications, and sepsis

We performed a linear regression analysis of the above factors and the percentages of sepsis and vasoactive drugs with the GMQ. The results showed that sepsis (β = −18.11,*P* = 0.003), PCIS (β = 0.55, *P* = 0.021) and IMV days (β = −0.736, *P* = 0.001) were independent risk factors for a decreased GMQ (*Table 2)*..

Discussion

The Infant and Toddler periods are vital times of gross motor development in human. Gross motor behavior is one of the earliest directly observable elements of adaptive function. At age 12 months, children begin learn to walk, and their functional connectivity of motor was correlated with walking[27]. During the toddler years, children are changing fastly in motor function and physical growth, and they increase the motor skills and ability to explore the environment[28]. Therefore, at this stage, factors such as diseases, environment or nutrition interfere with the chances of infants and young children receiving external information, which has a certain impact on their motor development. Uzark et al[29] found that gross motor impairments in infants after cardiac operations were common. Friedman et al[30] showed that young(ages 1–3 years) congenital diaphragmatic hernia survivors continue to have a high incidence of motor and language problems. Although the motor development dysfunction presents in the above populations, the motor development function level of children in the PICU is still unclear. In addition, children in PICU are more critically ill, undergo more invasive procedures, and use more drugs, so the level of motor development function in this part of the child is worthy of our attention. Unfortunately, few studies have focused on infants and toddlers in PICUs. This study is also the first to assess gross motor development function of PICU survivors.

In this study, the incidence of gross motor developmental dysfunction was 68.6%. This statistic is higher than the children after a cardiac operation(the incidence 21%–64%)[29, 31]. And the incidence of motor dysfunction was 60% in infants who survive congenital diaphragmatic hernia repair[30]. This may be due to the longer mechanical ventilation time, ICU hospital stay, and more complications in infants and toddlers of the PICU compared with those with post cardiac surgery. We believe that for critically ill children aged 1month to 3 years, assessing gross motor developmental function is more important in guiding subsequent rehabilitation.

We also found that IMV days were significantly longer in the dysfunctional group than in the non-dysfunctional group. This suggests that the length of IMV is related to the occurrence of gross motor developmental dysfunction. IMV is one of the most commonly used treatment methods in PICUs, but it causes many dysfunctions in motor, cognition and psychology despite saving the lives of critically ill children. At present, many adult studies have shown that IMV is a high risk factor for ICU-AW[32, 33]. Patel et al.[34] found that patients with ICU-AW had significantly longer mechanical ventilation times. A systematic review of published work showed evidence of ICU-AW in 46% (95% confidence interval [CI] 43–49%) of adult ICU patients who experienced lengthy mechanical ventilation, sepsis, or multiorgan failure[35]. However, the effects of mechanical ventilation on infants' gross motor development levels remain unreported. Our research showed that IMV days was associated with infants' gross motor developmental dysfunction. IMV is also accompanied by longer PICU stays, more sedative use, more severe protopathic conditions and more invasive examinations. Compared with the non- dysfunctional group, the length of PICU stay, days on sedatives, and days using CRRT were longer, and the vasoactive

drug use rate, sepsis incidence and PCIS score were higher in the dysfunctional group. These factors may promote gross motor developmental dysfunction in participants.

Therefore, our research linearly correlated the above factors with GMQ, and the results showed that the degree of gross motor dysfunction was significantly negatively correlated with PICU hospital stay, sedative use and CRRT days, and positively associated with PCIS scores. The GMQ of septic patients is also significantly lower than that of aseptic patients. To further analyze the independent risk factors that lead to gross motor developmental dysfunction, we performed a linear regression analysis of the above factors. The results showed that IMV days, sepsis and PCIS are independent risk factors for gross motor developmental dysfunction in PICU infants and toddlers. This is consistent with previous results of an adult study on ICU-AW. Jongheet al.[36] in their multicenter, prospective study showed that physical dysfunction in ICU patients is associated with prolonged mechanical ventilation. A prospective cohort study by Borges et al. indicated that physical activity, exercise capacity, and muscle strength of ICU sepsis survivors are significantly reduced, even at 3 months after discharge[37]. A meta-analysis conducted by Yang et al. incorporating 14 studies, showed that sepsis (OR, 2.2; 95%CI, 1.30–3.71) and duration of IMV (OR, 1.1; 95%CI, 1.00–1.22) were significantly associated with ICU-AW[38]. A multicenter study by Choong et al. suggested that Pediatric Risk of Mortality III (PRISM III) is an independent risk factor of social/cognitive dysfunction[39].

Our multivariate linear regression analysis showed that IMV days, sepsis and PCIS were independent risk factors for gross motor developmental dysfunction.This is similar to the results of several adult studies[40, 41]. We consider that the above risk factors leading to children's gross motor developmental dysfunction may have three pathways: 1. Prolonged mechanical ventilation and sepsis can lead to limb muscle atrophy[42, 43], resulting in weakened muscle strength in children; thus, abnormal assessment results may be due to weakened muscle strength; 2. Studies have confirmed that sepsis and IMV can cause brain dysfunction[44, 45]. However, the central nervous systems of infants and young children are still in the developmental stage, and motor neuron integrity is crucial to mastering children's motor skills. Therefore, damage to the child's motor center due to sepsis and IMV days may affect the overall motor development level; 3. Impairment of cognitive function is related to motor development dysfunction, and previous studies have confirmed the effects of sepsis and mechanical ventilation on cognitive function[42, 46, 47]. Impaired cognitive function factors can affect motor function in children, especially infants[48, 49]. Whether this phenomenon exists in infantile and toddler PICU survivors requires further study.

This study had several limitations. First, the study was an observational study with a small sample size. Therefore, we found that only IMV days, sepsis and PCIS differed statistically when performing linear regression analyses on related factors. Previous studies showed that hormone and sedative use were significantly associated with the occurrence of physical dysfunction in pediatric and adult patients[50–52].This study yielded in consistent results; therefore, more samples should be included for further analysis. Second, two assessment methods were used to assess the same patient pre-PICU and post-PICU. Due to the GMQ of the child before admission was not directly available, and only the ASQ–3

questionnaire could be used to indirectly reflect the gross motor function of the child. Third, our study only assessed the participants' motor development, while infant and toddler PICU survivors may have other developmental impairments such as cognitive, speech, psychological, and emotional disorders. Whether these dysfunctions are related to motor dysfunction warrants further study. Last, we did not follow up the enrollees to observe the gross motor function of these patients after discharge. In the next study we will further follow up this part of the patient.

In conclusion,this study showed gross motor developmental dysfunction in infantile and toddler PICU survivors are more common and may be exacerbated by experiences associated with longer IMV days and increasing illness severity combined with sepsis.

We suggest that early rehabilitative intervention in these children's gross motor developmental function may reduce physical morbidity. Furthermore, detailed comprehensive investigations of developmental functions, including gross motor, fine motor, language, cognition and social abilities, are warranted.

Abbreviations

PICU: pediatric intensive care unit; GMQ: gross motor quotient; ASQ–3: Age and Stages Questionnaires, Edition 3; PDMS–2: Peabody Developmental Motor Scales, Second Edition; IMV: invasive mechanical ventilation; ADLS: Activities of Daily Living Scale; NICU: neonatal intensive care unit; CRRT: continuous renal replacement therapy; PCIS: pediatric critical illness score; ICU-AW: intensive care unit-acquired weakness; MRC: MedicalResearch Council; PRISM III: Pediatric Risk of Mortality III

Declarations

Acknowledgements:

The authors wish to thank study site staff for their cooperation. The participation of parents and children in this study is greatly acknowledged.

Funding:

This work received no financial support.

Availability of data and materials:

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions:

Chun-FengYang conceived the study design and participated in study management. Yang Xue participated in the study design. Jun-Yan Feng and Yu Zhang performed statistical analyses. Fei-Yong Jia and Yu-Mei Li conceived and designed the study. All authors interpreted the data, contributed to the intellectual content, reviewed the manuscript, and approved the final version.

Ethics approval and consent to participate

The study was approved by the institutional ethics committee of the hospital, the First Hospital of Jilin University (ChiCTR1800020196). The parents or guardians of the eligible children provided written informed consent. An information sheet was provided for the parents or guardians of all the participants.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Author details

[1]Department of Pediatrics Intensive Care Unit, The First Hospital of Jilin University, Changchun, China

[2]Department of Developmental and Behavioral Pediatrics, The First Hospital of Jilin University, Changchun, China.

References

1.Field-Ridley, A, M Dharmar, D Steinhorn, et al. ICU-Acquired Weakness Is Associated With Differences in Clinical Outcomes in Critically Ill Children. Pediatr Crit Care Med, 2016. 17(1): 53–57.

2.Esses, SA, S Small, A Rodemann, et al. Post-Intensive Care Syndrome: Educational Interventions for Parents of Hospitalized Children. Am J Crit Care, 2019. 28(1): 19–27.

3.Newth, CJL, RG Khemani, PA Jouvet, et al. Mechanical Ventilation and Decision Support in Pediatric Intensive Care. Pediatr Clin North Am, 2017. 64(5): 1057–1070.

4.Als, LC, MD Picouto, SM Hau, et al. Mental and physical well-being following admission to pediatric intensive care. Pediatr Crit Care Med, 2015. 16(5): e141–149.

5.Pinto, NP, EW Rhinesmith, TY Kim, et al. Long-Term Function After Pediatric Critical Illness: Results From the Survivor Outcomes Study. Pediatr Crit Care Med, 2017. 18(3): e122-e130.

6.Colville, GA and CM Pierce. Children's self-reported quality of life after intensive care treatment. Pediatr Crit Care Med, 2013. 14(2): e85–92.

7.Herrup, EA, B Wieczorek, and SR Kudchadkar. Characteristics of postintensive care syndrome in survivors of pediatric critical illness: A systematic review. World J Crit Care Med, 2017. 6(2): 124–134.

8.Parry, SM, M Huang, and DM Needham. Evaluating physical functioning in critical care: considerations for clinical practice and research. Crit Care, 2017. 21(1): 249.

9.Schindler, MB. Prediction of ventilation weaning outcome: children are not little adults. Crit Care, 2005. 9(6): 651–652.

10.Hovels-Gurich, HH, MC Seghaye, S Dabritz, et al. Cognitive and motor development in preschool and school-aged children after neonatal arterial switch operation. J Thorac Cardiovasc Surg, 1997. 114(4): 578–585.

11.Subedi, D, MD DeBoer, and RJ Scharf. Developmental trajectories in children with prolonged NICU stays. Arch Dis Child, 2017. 102(1): 29–34.

12.Ricci, E, C Einspieler, and AK Craig. Feasibility of Using the General Movements Assessment of Infants in the United States. Phys Occup Ther Pediatr, 2018. 38(3): 269–279.

1. Byrne, E, Garber, J. Physical therapy intervention in the neonatal intensive care unit. Physical & Occupational Therapy in Pediatrics, 2013.33(1): 75–110.
2. Pollack, MM, Holubkov, R, Funai, T, Clark, A, Jenkins, TL. Pediatric intensive care outcomes: development of new morbidities during pediatric critical care. Pediatric Critical Care Medicine, 2014: 15(9).

15.Fay, D, T Wilkinson, AD Anderson, et al. Effects of Modified Instructions on Peabody Developmental Motor Scales, Second Edition, Gross Motor Scores in Children with Typical Development. Phys Occup Ther Pediatr, 2019: 1–13.

16.Tso, WWY, VCN Wong, X Xia, et al. The Griffiths Development Scales-Chinese (GDS-C): A cross-cultural comparison of developmental trajectories between Chinese and British children. Child Care Health Dev, 2018. 44(3): 378–383.

17.Zhang, L, H Huang, Y Cheng, et al. Predictive value of four pediatric scores of critical illness and mortality on evaluating mortality risk in pediatric critical patients. Zhonghua Wei Zhong Bing Ji Jiu Yi Xue, 2018. 30(1): 51–56.

18.Fan, XM and PT Collaborative Group for Simplified. Clinical application of simplified pediatric critical illness scoring system. Zhong hua Er Ke Za Zhi, 2003. 41(8): 565–569.

19.Halbwachs, M, JB Muller, S Nguyen The Tich, et al. Usefulness of parent-completed ASQ for neurodevelopmental screening of preterm children at five years of age. PLoS One, 2013. 8(8): e71925.

20.Steenis, LJ, M Verhoeven, DJ Hessen, et al. Parental and professional assessment of early child development: the ASQ–3 and the Bayley-III-NL. Early Hum Dev, 2015. 91(3): 217–225.

21.Marks, KP, N Madsen Sjo, and P Wilson. Comparative use of the Ages and Stages Questionnaires in the USA and Scandinavia: a systematic review. Dev Med Child Neurol, 2018.

22.Saraiva, L, LP Rodrigues, R Cordovil, et al. Motor profile of Portuguese preschool children on the Peabody Developmental Motor Scales–2: a cross-cultural study. Res Dev Disabil, 2013. 34(6): 1966–1973.

23.Tavasoli, A, P Azimi, and A Montazari. Reliability and validity of the Peabody Developmental Motor Scales-second edition for assessing motor development of low birth weight preterm infants. Pediatr Neurol, 2014. 51(4): 522–526.

24.Glass, TJA, V Chau, RE Grunau, et al. Multiple Postnatal Infections in Newborns Born Preterm Predict Delayed Maturation of Motor Pathways at Term-Equivalent Age with Poorer Motor Outcomes at 3 Years. J Pediatr, 2018. 196: 91–97 e1.

25.Wang, HH, HF Liao, and CL Hsieh. Reliability, sensitivity to change, and responsiveness of the peabody developmental motor scales-second edition for children with cerebral palsy. Phys Ther, 2006. 86(10): 1351–1359.

26.Maddox, Taddy. Peabody Developmental Motor Scales. Second Edition. Encyclopedia of Special Education, 2008.

1. Marrus, N. Eggebrecht, A. T, Todorov, A, Elison, JT, Wolff, JJ, Cole, L, et al. Walking, gross motor development, and brain functional connectivity in infants and toddlers. Cerebral Cortex, 2018. 28(2), 750–763
2. Colson, ER, Dworkin, PH. Toddler development. Pediatrics in Review, 1997. 18(8), 255–259.
3. Uzark, K, Smith, C, Donohue, J, Yu, S, Romano, JC. Infant motor skills after a cardiac operation: the need for developmental monitoring and care. The Annals of Thoracic Surgery, 2017. S0003497516318902.
4. Friedman, S, Chen, C, Chapman, JS, Jeruss, S, Terrin, N, Tighiouart, H, et al. Neurodevelopmental outcomes of congenital diaphragmatic hernia survivors followed in a multidisciplinary clinic at ages 1 and 3. Journal of Pediatric Surgery, 2008. 43(6), 0–1043.

5. Hamrick, SEG, Gremmels, DB, Keet, CA, Leonard, CH, Connell, JK, Hawgood, S, et al. Neurodevelopmental outcome of infants supported with extracorporeal membrane oxygenation after cardiac surgery. Pediatrics, 2003. 111(6 Pt 1), e671–5.

32.Friedrich, O, MB Reid, G Van den Berghe, et al. The Sick and the Weak: Neuropathies/Myopathies in the Critically Ill. Physiol Rev, 2015. 95(3): 1025–1109.

33.Larsson, L and O Friedrich. Critical Illness Myopathy (CIM) and Ventilator-Induced Diaphragm Muscle Dysfunction (VIDD): Acquired Myopathies Affecting Contractile Proteins. Compr Physiol, 2016. 7(1): 105–112.

34.Patel, BK, AS Pohlman, JB Hall, et al. Impact of early mobilization on glycemic control and ICU-acquired weakness in critically ill patients who are mechanically ventilated. Chest, 2014. 146(3): 583–589.

35.Latronico, N and CF Bolton. Critical illness polyneuropathy and myopathy: a major cause of muscle weakness and paralysis. Lancet Neurol, 2011. 10(10): 931–941.

36.De Jonghe, B, T Sharshar, JP Lefaucheur, et al. Paresis acquired in the intensive care unit: a prospective multicenter study. JAMA, 2002. 288(22): 2859–2867.

37.Borges, RC, CR Carvalho, AS Colombo, et al. Physical activity, muscle strength, and exercise capacity 3 months after severe sepsis and septic shock. Intensive Care Med, 2015. 41(8): 1433–1444.

38.Yang, T, Z Li, L Jiang, et al. Risk factors for intensive care unit-acquired weakness: A systematic review and meta-analysis. Acta Neurol Scand, 2018. 138(2): 104–114.

39.Choong, K, D Fraser, S Al-Harbi, et al. Functional Recovery in Critically Ill Children, the “WeeCover” Multicenter Study. Pediatr Crit Care Med, 2018. 19(2): 145–154.

40.Mehta, AB, AJ Walkey, D Curran-Everett, et al. Hospital Mechanical Ventilation Volume and Patient Outcomes: Too Much of a Good Thing? Crit Care Med, 2019. 47(3): 360–368.

41.Arah, OA. Hospital volume and outcomes of mechanical ventilation. N Engl J Med, 2006. 355(15): 1617; author reply 1617–1619.

42.Ji, M, H Yuan, S Yuan, et al. The p75 neurotrophin receptor might mediate sepsis-induced synaptic and cognitive impairments. Behav Brain Res, 2018. 347: 339–349.

43.Baldwin, CE and AD Bersten. Myopathic characteristics in septic mechanically ventilated patients. CurrOpin Clin Nutr Metab Care, 2015. 18(3): 240–247.

44.Adam, N, S Kandelman, J Mantz, et al. Sepsis-induced brain dysfunction. Expert Rev Anti Infect Ther, 2013. 11(2): 211–221.

45.Sonneville, R, F Verdonk, C Rauturier, et al. Understanding brain dysfunction in sepsis. Ann Intensive Care, 2013. 3(1): 15.

46.Girard, TD, JL Thompson, PP Pandharipande, et al. Clinical phenotypes of delirium during critical illness and severity of subsequent long-term cognitive impairment: a prospective cohort study. Lancet Respir Med, 2018. 6(3): 213–222.

47.Patel, MB, A Morandi, and PP Pandharipande. What's new in post-ICU cognitive impairment? Intensive Care Med, 2015. 41(4): 708–711.

48.Champion, JA, KJ Rose, JM Payne, et al. Relationship between cognitive dysfunction, gait, and motor impairment in children and adolescents with neurofibromatosis type 1. Dev Med Child Neurol, 2014. 56(5): 468–474.

49.Al-Nemr, A and F Abdelazeim. Relationship of cognitive functions and gross motor abilities in children with spastic diplegic cerebral palsy. Appl Neuropsychol Child, 2018. 7(3): 268–276.

50.Meduri, GU, A Schwingshackl, and G Hermans. Prolonged Glucocorticoid Treatment in ARDS: Impact on Intensive Care Unit-Acquired Weakness. Front Pediatr, 2016. 4: 69.

51.Taipale, HT, JS Bell, D Gnjidic, et al. Muscle strength and sedative load in community-dwelling people aged 75 years and older: a population-based study. J Gerontol A Biol Sci Med Sci, 2011. 66(12): 1384–1392.

52.Tomita, S, N Matsuura, and T Ichinohe. The combined effects of midazolam and propofol sedation on muscle power. Anaesthesia, 2013. 68(5): 478–483.

Tables

Table 1 Participants Study Cohort Characteristics

Characteristics	Dysfunction Group (n=24)	Non- Dysfunction Group (n=11)	*P*
Age, months (mean±SD)	20.9±12.4	15.6±12.9	**0.005**
Male sex (%)	58.3	63.6	0.766
Reason for admission (%)			
Cardiovascular	8.3	9.3	0.941
Respiratory	83.3	81.8	0.912
Gastrointestinal	8.3	9.1	0.941
PCIS (mean±SD)	81.08±9.09	92.18±5.17	**0.001**
PICU length of stay, d, median (IQR)	22.50(14.50–27.75)	9.00(7.00–17.00)	**0.029**
Use of vasoactive medications, n (%)	57.9	8.3	**0.006**
IMV days(mean±SD)	7.46±5.34	1.27±2.83	**0.001**
Sedative days, d, median (IQR)	8.50(2.50–13.75)	2.0(1.0–7.0)	**0.021**
Methylprednisolone, d, median (IQR)	5.5(4.25–7.75)	3.00(0.00–7.00)	0.130
CRRT days, d, median (IQR)	3.50(0.00–7.00)		
Sepsis (%) 20.8	9.1	**<0.001**	
Surgical, n (%) 8.3			

IQR = interquartile range; **SD** = standard deviation; **PCIS** = pediatric critical illness score; **CRRT** = continuous renal replacement therapy; **IMV** = invasive mechanical ventilation; **GMQ** = gross motor quotient

Table 2. Linear regression analysis of risk factors associated with GMQ

Factors	Gross Motor Quotient		
	β	**Se(β)**	***P***
IMV days	-0.736	0.260	**0.001**
Sepsis	**-**18.110	0.414	**0.003**
PCIS	0.550	0.338	**0.021**

The risk factors included in the linear regression analysis were **length of PICU stay**, **days on sedatives, IMV days, CRRT days, PCIS, use of vasoactive medications** and **sepsis.**

Figures

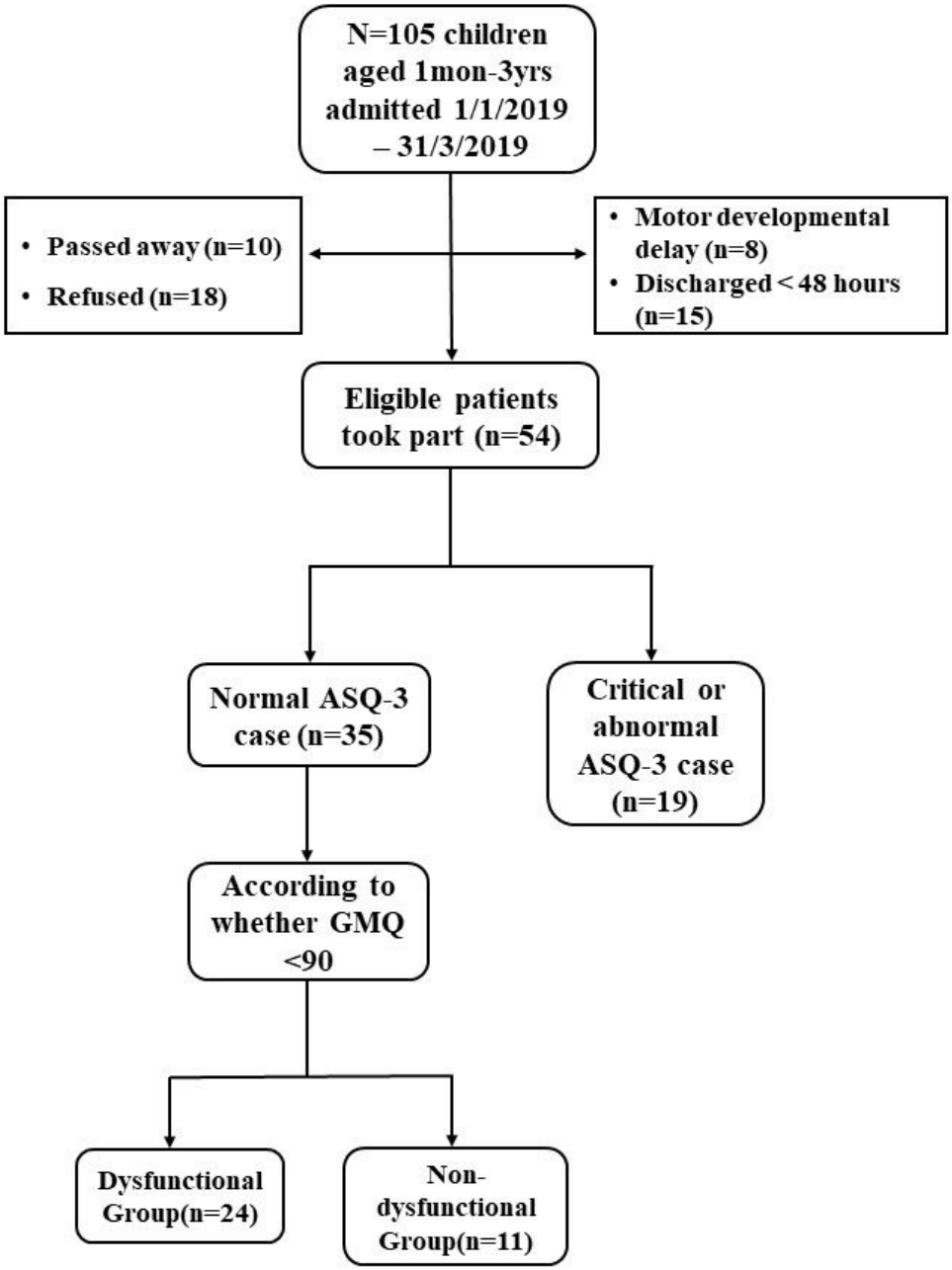

Figure 1

Flow chart for the study.

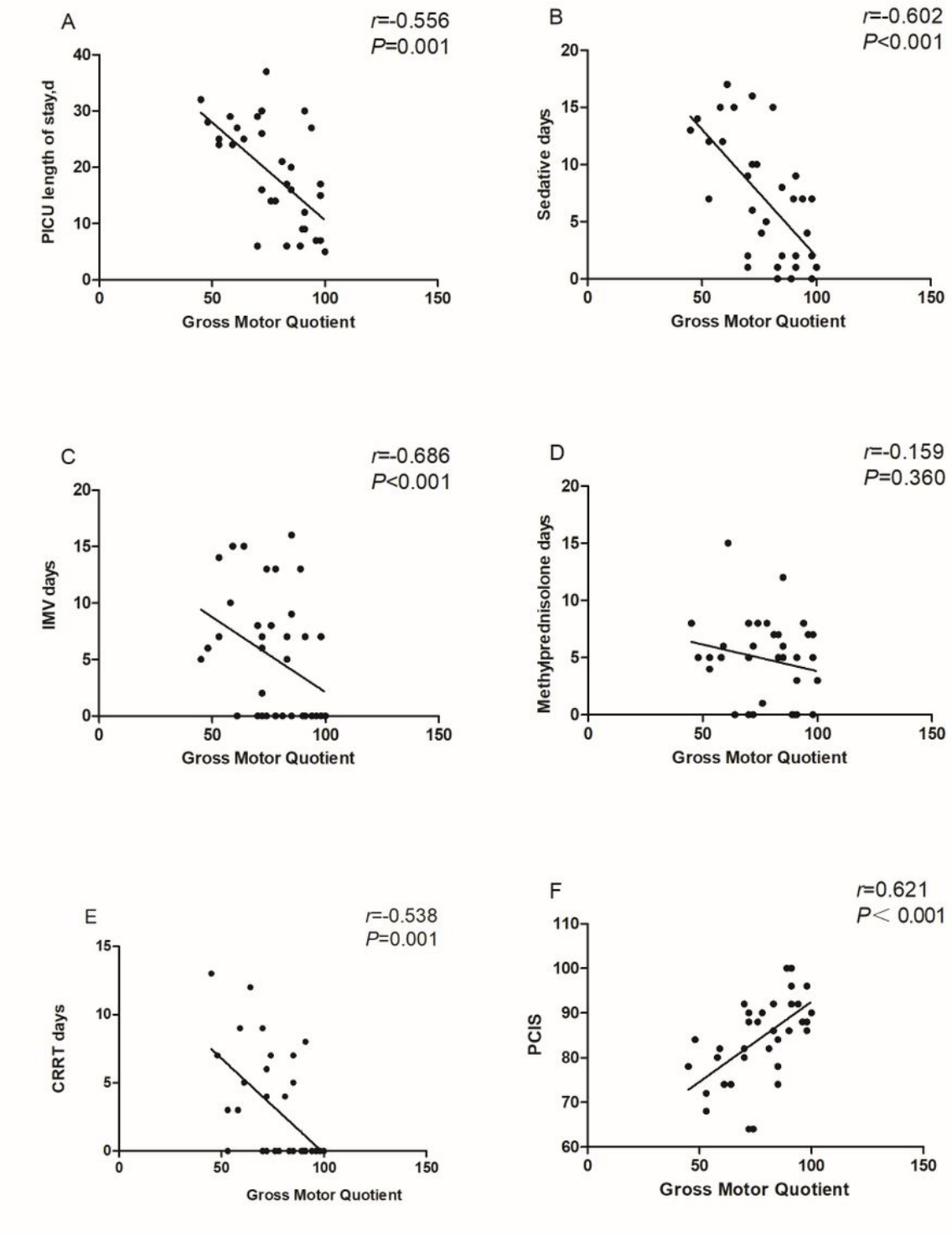

Figure 2

Spearman's correlation test was used to evaluate the relationships between GMQ and length of PICU stay, days on sedatives, IMV days, days on methylprednisolone, CRRT days and PCIS, respectively