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# Pediatric acute respiratory distress syndrome and new pediatric outcomes

**Source:** Keim, G; Watson, RS; Thomas NJ; Yehya, N. New Morbidity and Discharge Disposition of Pediatric Acute Respiratory Distress Syndrome Survivors. *Crit Care Med* 2018; 46:1731-1738.

**P**ediatric acute respiratory distress syndrome (PARDS) causes significant disease burden in Pediatric Intensive Care Units (PICUs) with a reported prevalence of close to 3%<sup>1</sup> and short-term mortality rates up to 20%<sup>2</sup>. However, following PICUs tendency to exchange higher mortality rates for higher morbidity rates, PARDS research needs to focus on data about survivors and mortality cannot be the only outcome.

The article uses a scale created as an outcome measure for use in pediatric research called the Functional Status Scale (FSS). New morbidity is defined as a 3 point increase in the scale. The authors aimed to determine new morbidity rate using change in FSS, hospital discharge disposition and 1 and 3 year mortality for survivors of PARDS. Also, researchers tried to establish epidemiologic, physiologic and treatment factors associated with these outcomes.

The cohort consisted of consecutive PICU patients from the Children's Hospital of Philadelphia's (CHOP), eligible between July 1, 2011 and December 31, 2014, who met the former criteria for Acute Lung Injury. There is a new definition for PARDS since 2015, but all patients would even though meet this diagnosis. The following data were collected in the study: demographics data, Pediatric Risk of Mortality (PRISM) III, preillness FSS and at hospital discharge, ventilator settings and Pao<sub>2</sub>/Fio<sub>2</sub> at PARDS onset and 24 hours, laboratory data, medications for the first 3 days of PARDS and nonpulmonary organ failures at time of PARDS diagnosis. The main outcome was status at hospital discharge, trichotomized to alive without new morbidity, alive with new morbidity, and dead.

Among the 316 patients diagnosed with PARDS, the inhospital mortality rate was 13,3%. Survivors accounted for 274 patients – 77% survived without new morbidity and 23% survived with new morbidity. Those outcomes correlated well with severity of illness, non-pulmonary organ failures and severity of PARDS at 24 hours. There was a stepwise increase in each of these severity of illness markers, with survivors without new morbidity demonstrating better values, non-survivors the worst, and survivors with new morbidity having intermediate values. They divide the outcomes as good (alive without new morbidity) versus poor (new morbidity or death), and poor outcome was associated with PRISM III, nonpulmonary organ failures, immunocompromising comorbidities, and oxygenation and ventilator pressures 24 hours after PARDS onset.

Within the survivors, 72,3% were discharged home, 24,5% needed rehabilitation and 3,3% were transferred to chronic care facilities. A FSS greater than

or equal to 3 was strongly associated with discharge to rehabilitation, with highest declines in feeding, motor and respiratory functional domains. Regarding respiratory outcomes, 20,4% (56 patients) of hospital survivors had change in FSS. Of these, 19 patients underwent tracheostomy placement. Of the 56 patients with a change in respiratory FSS, 17 (30.4%) had improvement in their respiratory FSS by 3-year follow-up, 10 (17.9%) had returned to a nonmorbid FSS of 1, but seven died within the first year after PARDS and one additional patient died by 3-year follow-up. One and three-year mortality were 5,5% and 8%, respectively. One- and 3-year mortality in survivors of PARDS was most strongly predicted by immunocompromised status and higher baseline FSS, with weaker association with PRISM III score, suggesting baseline disease would influence more than PARDS itself to the prognosis.

**Commentary by:** Ana Cecília Aziz, MD.  
Pediatric Intensivist at Complexo Hospitalar de Niterói,  
Hospital Getúlio Vargas Filho and Hospital Copa D'Or.

The issue discussed in this article is extremely important, since PARDS continues to be an important syndrome in PICU, affecting 3%<sup>1</sup> of PICUs patients. With increasing technology, advances in the use of extracorporeal membrane oxygenation (ECMO), protective ventilatory strategies and understanding of PARDS pathophysiology, mortality has lowered and survival with new morbidities is becoming a more robust outcome to be measured. The FSS is a functional status outcome measure for large studies that is well defined, quantitative, rapid, reliable, objective and suitable for a wide spectrum of ages. It includes 6 domains: mental status, sensory, communication, motor, feeding and respiratory, categorized from normal (1) to very severe dysfunction (5)<sup>3</sup>.

It is the first study relating PARDS and functional outcomes. The authors showed that variables associated with inhospital mortality also related to new morbidity and new morbidity exists on an intermediate step along the continuum of intact survival to death. FSS seems to be a useful outcome measure in PARDS. These results confirm previous findings from a large study from Pollack et al<sup>4</sup>, which showed that increasing PRISM III scores was also associated with development of new morbidity and that new morbidity was a more common outcome than mortality<sup>5</sup>.

A cornerstone of improving critical care is early mobilization and rehabilitation<sup>6,7</sup>. CHOP had a well-developed rehabilitation center and the integration of early physical therapy services and an active rehabilitative medicine team with an associated inpatient rehabilitation unit may have contributed to better outcomes without new morbidity and early return to basal FSS after hospital discharge. Follow-up FSS scores would be helpful in knowing the effect of the rehabilitation interventions on the dysfunction associated with PARDS.

Finally, detecting new morbidities allows for the study of new interventions to reduce the consequences of PICU hospitalization, not only related to the disease itself, but also to the intensive care provided, making studies like these increasingly important.



## References

1. Khemani RG, Smith L, Lopez-Fernandez YM, Kwok J, Morzov R, Klein MJ, Yehya N, Willson D, Kneyber MCJ, Lillie J, Fernandez A, Newth CJL, Jouvet P, Thomas NJ; Pediatric Acute Respiratory Distress syndrome Incidence and Epidemiology (PARDIE) Investigators; Pediatric Acute Lung Injury and Sepsis Investigators (PALISI) Network.; Pediatric acute respiratory distress syndrome incidence and epidemiology (PARDIE): an international, observational study. *Lancet Respir Med*. 2018 Oct 22. pii: S2213-2600(18)30344-8.
2. Yehya N, Bhalla AK, Thomas NJ, et al: Alveolar dead space fraction discriminates mortality in pediatric acute respiratory distress syndrome. *Pediatr Crit Care Med* 2016; 17:101-109.
3. Pollack MM, Holubkov R, Glass P., Dean JM, Meert KL, Zimmerman J, Anand KJS, Carcillo J, Newth CJL, Harrison R, Willson DF, Nicholson C and the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) Collaborative Pediatric Critical Care Research Network (CPCCRN); The Functional Status Score (FSS): A New Pediatric Outcome Measure. *Pediatrics*. 2009 July ; 124(1): e18-e28.
4. Pollack MM, Holubkov R, Funai T, et al. Simultaneous prediction of new morbidity, mortality, and survival without new morbidity from pediatric intensive care: a new paradigm for outcomes assessment. *Crit Care Med* 2015;43(8):1699-709.
5. Pollack MM, Holubkov R, Funai T et al. for the Eunice Kennedy Shriver National Institute of Child Health and Human Development Collaborative Pediatric Critical Care Research Network. Pediatric Intensive Care Outcomes: Development of New Morbidities During Pediatric Critical Care. *Pediatr Crit Care Med* 2014; 15:821-827.
6. Wiecek B., Burke C., Al-Harbi A., Kudchadkar SR. Early mobilization in the pediatric intensive care unit: a systematic review; *J Pediatr Intensive Care*. 2015; 2015: 129-170. doi:10.1055/s-0035-1563386.
7. Hopkins RO, Choong K, Zebuhr CA, Kudchadkar SR. Transforming PICU Culture to Facilitate Early Rehabilitation. *J Pediatr Intensive Care*. 2015;4(4):204-211.



# Gender dysphoria and gender change in disorders of sex development. Impacts on early surgery indication.

**Source:** Kreukels, Baudewijntje P.C.Köhler, Birgit et al. Gender Dysphoria and Gender Change in Disorders of Sex Development/Intersex Conditions: Results From the dsd-LIFE Study. *The Journal of Sexual Medicine*, Volume 15, Issue 5, 777 - 785.

**T**he dsd-LIFE Study is a multicentric European study on the outcome of surgical, hormonal therapy and psychological intervention in disorders of sex development (DSD). The aim of this publication is to assess gender change and gender dysphoria with a cross-sectional study in 14 different centers with 1,040 participants.

Gender assignment is realized at birth solely based on the appearance of the external genitalia. The authors discuss how sometimes that may not be congruent to how one identifies oneself gender, and some of its implications. When a significant psychological distress is present, a diagnosis of gender dysphoria is made. For some people that develop the opposite gender identity (transgender), to be socially accepted as a person of the other gender might suffice, but others might need health care.

Many factors might influence the expressed gender through life, and the exposure to androgens pre- and postnatal has been shown to have a role on male behavior, which is significant for DSD treatment, particularly with 46,XY children. This study includes a variety of diagnosis, Turner and Klinefelter syndromes, congenital adrenal hyperplasia (CAH) and XY DSD.

Participants should be at least 16 years old, have a confirmed DSD diagnosis and consent to participate. They had a medical clinical interview and filled patient-report outcome (PRO) questionnaires, and clinical retrospective data were collected. Of the 3,217 invited, 1,040 (36.1%) were included.

The PRO questionnaires included the Rosenberg Self-Esteem Scale and a shortened version of the Utrecht Gender Dysphoria Scale. Both male and female versions were offered to the participant to choose the most appropriate.

Patients were organized in 6 main groups based on their current gender and kind of diagnosis and 47 (5.1%) of them had a gender change, but most of them, 36, had it done before puberty, probably based on clinical decision. Only 9 (8 in some XY group and 1 in the CAH group) had a postpubertal (probably a patient decision) change. The highest incidence of patient-initiated gender change was seen in the XY group, with androgen effect. Of 78 male-raised individuals, 2 (2.6%) changed gender, as opposed to 5 of 58 (8.6%) of the female-raised individuals. Eighteen individuals were not in the main groups (5 CAH), and 5 of them had a postpubertal change, so a total of 14 (1.3%) had a gender change.

Compared to a control group, only 5 individuals of the main group (3 Turner, 1 Klinefelter, 1 CAH) had a GD score higher than 3 SD above the mean. The ones that changed gender probably had GD before the transition.

Depending on the source of info (clinical interview or PRO), gender variance or non-binary gender expression rate was from 12 (1%) to 27 (2.6%). They had lower self-esteem, more anxiety and depression, and more gender dysphoria when compared to the gender-typical group. This later was below the GD found in non DSD gender

identity clinics. When considering partnership and sexuality there was no significant difference when comparing both groups scores.

Only 1% (3% if Turner and Klinefelter are excluded) DSD patients sought gender change after puberty, a low number, even if higher than what is found in the general population (up to 0.7%). Of the patients that had gender change during early childhood (since 2006 the age of 18 months is seen as an upper limit) without the patient input, only 1 transitioned back. As expected, the female to male change rate was higher in the XY group exposed to androgens, but the incidence of gender changes in the 5-a-RD-2 and 17-b-HSD-3 individuals was way lower than the literature reports, probably because in western societies (as the ones where the study was done), one can more freely accept a gender role that is different from the one assigned at birth. The presence of the DSD itself may cause some confusion and discomfort, even in individuals that have no desire whatsoever to change gender or role. Results also show that people in the gender fluid group had more gender related distress, anxiety and lower self-esteem, but lower than non DSD individuals seeking gender identity clinics.

**Commentary by:** Andre Cunha, MD.  
Division of Pediatric Surgery, IPPMG,  
The Federal University of Rio de Janeiro.

The surgical treatment of DSDs has evolved through the decades, from a simple anatomical adequacy of the external genitalia to the gender assigned at birth (as seen with the clitoris resection surgeries), to techniques concerned with sexual function and satisfaction as described by Passerini-Glazel<sup>1</sup>. Recently there is concern in allowing future anatomic reversibility, as proposed by Pippi-Salle<sup>2</sup>, but the feasibility of this approach has yet to be shown. Moving in the same direction, those decisions were taken from a single physician to a multi-disciplinary team with involvement of the parents<sup>3</sup>.

The dsd-LIFE study helps in shedding some light and numbers on a very controversial topic that has been contaminated by political, ideological and sexual orientation issues. Some activist movements, as interACT (<https://interactadvocates.org/>), pleas for a ban on all DSD patients surgeries until they can provide an informed consent, while others as CARES (<https://www.caresfoundation.org/>), fight to preserve CAH patient and parental right. Meanwhile bills like California SB-201<sup>4</sup> are being passed. As the dsd-LIFE study shows that all different diagnosis do not have the same outcome and probably should be assessed in different ways.

## References

1. Passerini-Glazel G. A new 1-stage procedure for clitorovaginoplasty in severely masculinized female pseudohermaphrodites. *J Urol* 1989;142:565-8.
2. Pippi Salle JL, Braga LP, Macedo N, Rosito N, and Bagli D. Corporeal sparing dismembered clitoroplasty: an alternative technique for feminizing genitoplasty. *Journal of Urology*, vol. 178, no. 4, pp. 1796-1801, 2007.
3. Douglas G, Axelrad ME, Brandt ML, Crabtree E, Dietrich JE, French S, Gunn S, Karaviti L, Lopez ME, Macias CG, McCullough LB, Suresh D, Sutton VR. Consensus in guidelines for evaluation of DSD by the Texas Children's Hospital Multidisciplinary Gender Medicine Team. *Int J Pediatr Endocrinol*. 2010;2010:1-17.
4. Leginfo.legislature.ca.gov. (2019). Bill Text - SB-201 Medical procedures: treatment or intervention: sex characteristics of a minor. [online] Available at: [https://leginfo.legislature.ca.gov/faces/billTextClient.xhtml?bill\\_id=201920200SB201](https://leginfo.legislature.ca.gov/faces/billTextClient.xhtml?bill_id=201920200SB201) [Accessed 5 Mar. 2019].

# Opioid weaning in critically ill children

**Source:** Sanchez-Pinto LN, Nelson LP, Lieu P, Koh J, Rodgers J, Larson K, Huson J, Amirnovin R. Implementation of a risk-stratified opioid weaning protocol in a pediatric intensive care unit J Crit Care 2018; 43:214-219.

**T**his study aimed to implement a risk-stratified opioid weaning protocol. Its rationale is to reduce the duration of opioid use in the care of critically ill children without increasing the incidence of withdrawal syndrome. It was prospectively conducted in a large children's hospital pediatric intensive care unit (PICU) with 107 children younger than 21 years of age who received scheduled opioids for at least seven days during their admission to the PICU. The 24-bed tertiary PICU serves a wide range of patients: medical, surgical, trauma, and solid-organ and hematopoietic stem cell transplantation patients, but not postoperative cardiac patients. Two groups of patients were compared: pre and post-protocol implementation. In the pre-intervention period, opioid weaning was at the discretion of the treating physicians.

To apply the weaning protocol, the authors first used an algorithm to stratify each patient risk of withdrawal in low, moderate, high or very high. The opioid infusion dose was then converted to a weaning medication (either intravenous hydromorphone or oral methadone, according to the patient's risk of withdrawal), and withdrawal signs and symptoms were assessed regularly using the Withdrawal Assessment Tool (WAT-1). The primary outcome was duration of opioid exposure, measured using the total length of scheduled opioids and the length of opioid weaning. Total exposure to opioids was also calculated as cumulative morphine equivalents (mg/Kg/patient) from initiation of opioids until the last dose of scheduled weaning opioid. The secondary outcomes included hospital length of stay, number of patients discharged home on opioids, and protocol compliance.

The mean age was similar in both groups: 2.1 and 2.3 years in the pre and post-intervention groups respectively. In the post-intervention group, 15 patients (38%) met moderate-risk, 23 patients (59%) met high-risk, and 1 patient (3%) met very high-risk for withdrawal criteria. Protocol implementation decreased the total length of scheduled opioids, the length of opioid weaning and total exposure to opioids (33.2 vs 48.8 mg/kg/patient,  $p=0.02$ ). The reduction in hospital length of stay in the post-intervention group was not statistically significant. The number of patients discharged home on opioids was not different. Protocol compliance in the post-intervention group was very high. Protocol-driven opioid weaning did not increase adverse events such as withdrawal symptoms, rescue opioid or naloxone doses or unplanned extubations.

The authors conclude that the purpose of the protocol implementation, that is, reducing opioid exposure without increasing opioid withdrawal syndrome, was achieved, which is consistent with previous studies. They highlight the importance of monitoring withdrawal signs and symptoms in the advance of the weaning protocol, especially for those patients who present withdrawal signs or symptoms from other causes. Risk stratification ensures a tailored approach for each patient, increasing the chances of successful weaning as well as maximizing protocol acceptability by health care professionals.

**Commentary by:** Leticia Massaud-Ribeiro, MD.  
Pediatrician and Pediatric Intensive Care Specialist.

This is a large study that tested the use of an opioid weaning protocol in various profiles of critically ill children, except for cardiac surgery patients. Nevertheless, this population of postoperative cardiac patients was tested separately by the same research group with a similar study design and results, but with statistically significant reduction in hospital length of stay.<sup>1</sup> So results can overall be considered consistent. However, both are single-center studies and need to be replicated externally for the results to be validated.

One particular aspect that needs to be pointed out is that there was no other weaning protocol before the implementation of this risk-stratified opioid weaning protocol. Weaning, as well as sedation, was at the discretion of the treating physician. It is possible that the intervention in this study that most influenced the outcomes was the implementation of the protocol itself, regardless of its methods, since there was absolutely no recommendation to physicians before. The absence of a sedation protocol, however, does not seem to have influenced the results, since exposure to adjunct medications was similar between groups.

In general, intensive care interventions are associated with better outcomes when driven by protocols rather than at the discretion of the bedside team. Improvements in outcomes have been similarly demonstrated for other widely used interventions, such as sedation,<sup>2</sup> neuromuscular blockade,<sup>3,4</sup> mechanical ventilation weaning<sup>5</sup> and, most notably, sepsis management.<sup>6</sup> Sedation and analgesia management outcomes are closely related to opioid weaning. Current recommendations favor the use of goal-directed sedation protocols, which can decrease opioid exposure and, as a result, duration of the opioid weaning phase, with less withdrawal signs and symptoms.

Sedation and analgesia management in particular is a widely variable intervention across PICUs. Apart from all the outcome benefits of protocol-driven care, the use of goal-directed sedation and weaning protocols reduces variability of these practices within the PICU, making it more uniform and rendering practitioners more conscious of the risks and benefits of their management decisions, putting the clinical knowledge base developed in the protocol into everyday practice.

## References

1. Amirnovin R, Sanchez-Pinto LN, Okuhara C, Lieu P, Koh JY, Rodgers JW, Nelson LP. Implementation of a Risk-Stratified Opioid and Benzodiazepine Weaning Protocol in a Pediatric Cardiac ICU *Pediatr Crit Care Med* 2018; 19(11):1024-1032.
2. Harris J, Ramelet AS, van Dijk M, Pokorna P, Wielenga J, Tume L, Tibboel D, Ista E. Clinical recommendations for pain, sedation, withdrawal and delirium assessment in critically ill infants and children: an ESPNIC position statement for healthcare professionals *Intensive Care Med* 2016; 42(6):972-986.
3. Playfor S, Jenkins I, Boyles C et al. Consensus guidelines for sustained neuromuscular blockade in critically ill children *Paediatr Anaesth* 2007; 17:881-887.
4. Murray MJ, DeBlock H, Erstad B et al. Clinical Practice Guidelines for Sustained Neuromuscular Blockade in the Adult Critically Ill Patient *Crit Care Med* 2016; 44:2079-2103.
5. Jordan J, Rose L, Dainty KN, Noyes J, Blackwood B. Factors that impact on the use of mechanical ventilation weaning protocols in critically ill adults and children: a qualitative evidence-synthesis (Review) *Cochrane Database Syst Rev* 2016; 10:CD011812.
6. Davis AL, Carcillo JA, Aneja RK et al. American College of Critical Care Medicine Clinical Practice Parameters for Hemodynamic Support of Pediatric and Neonatal Septic Shock *Crit Care Med* 2017; 45(6):1061-1093.

# Adolescents have a better overall survival when treated in pediatric oncology centers?

**Source:** Emmanuel Desandes, Laurence Brugieres, Valérie Laurance, Claire Berger, Justyna Kanold, Isabelle Tron, Jacqueline Clavel, Brigitte Lacour. Survival of adolescents with cancer treated at pediatric versus adult oncology treatment centers in France. 21 September 2016. DOI: 10.1002/pbc.26326.

**T**he study was conducted at the French National Registry of Childhood Solid Tumor, University Hospital Nancy, in France. It observed adolescent patients (15-19 years of age), living in one of the six French administrative regions, diagnosed with any type of cancer or with Central Nervous System tumor between January 1, 2006, and December 31, 2007.

Each patient's data was collected from their medical records, and included gender, age at diagnosis, type of cancer, time to diagnosis, time to start the treatment, management in the context of a multidisciplinary decisional approach, inclusion in clinical studies and the type of cancer treatment center (adult or pediatric). The initial time was the date of the diagnosis and the final time was considered the death event. The length of follow-up ranged from 0 to 84 months, averaging 69 months.

Several previous studies have shown that adolescents and young adults treated at a pediatric oncology center have better survival outcomes than those treated at an adult oncology facility. The objectives of the study were to identify which factors influence the access to each type of care (adult and pediatric) and which determine the effect of the treatment center on survival rates.

Along two years of study, 594 patients aged 15-19 years were diagnosed with cancer. Of this total, 33% were managed at a pediatric center and 67% at an adult center. The study shows that younger patients were more likely to be treated at a pediatric center, while older patients were more likely to be treated at an adult center.

Adolescents with sarcoma or leukemia were more likely to be treated at a pediatric center, while patients with carcinoma/melanoma or germ-cell tumor were more likely to be treated at an adult center. The proportional of metastatic tumors and intracranial or intraspinal embryonal tumors (including tumors associated with poor outcomes) was higher for patients treated at pediatric centers than those treated at adult centers.

The proportion of males and females was the same. Adolescents with central nervous system tumor managed at an adult center had a longer time to diagnosis. For all cancers taken together, no differences were observed for time to treatment. However, adolescents with leukemia and lymphoma had a shorter time to treatment when they were treated at a pediatric center. Management decisions, especially the decision to initiate treatment, were taken by a multidisciplinary team in 53,9% of cases (the percentage was higher for patients treated at pediatric centers). Adolescents treated at pediatric centers were more frequently included in clinical studies.



At the end of the follow up, 107 adolescents (18%) died on an average rate of 22 months (between diagnosis and death). For all cancers of any site, the overall survival was 94,1% at 1 year and 81,9% at 5 years. High 5-year overall survival was observed for Germ cell tumor, carcinomas and melanomas, Hodgkin lymphomas, central nervous system tumors, and Non Hodgkin lymphoma. Low 5 year overall survival was observed for malignant bone tumors, acute myeloid leukemia, and soft tissue sarcomas.

Unlike previous studies, the article shows that the overall survival rates for adolescent patients diagnosed with any kind of cancer treated at a pediatric center or adult center did not differ. The 5-years overall survival in adolescents has improved from 72% during the 1988-1997 period to 81,2% during the study period.

**Commentary by:** Luiza Feuillatey Albagli, MD.  
Pediatric Hematologist, Master Student at IPPMG/UFRJ.

The better survival rates over time probably can be justified by the improvement of chemotherapy, the new technologies and a more prepared intensive care.

In this study, patients were not stratified by the prognostic risk; they were heterogeneous in relation to the risk classification. Therefore, the chance of death was not the same for all the patients, even the ones with the same cancer. This may disrupt the results, because if the majority of patients with worse prognosis were treated at the pediatric center, the overall survival of this treatment center would be lower. Besides that, the relatively small number of patients (594 cases) over a short period of study (2006-2007), limited the power of the analysis.

Although the study has not covered all the country, 41% of the whole country is a good sample. The time of the follow up is adequate because the average was 69 months (5,7 years) and the authors want to see the overall survival in 5 years.

This study was very important because adolescents are a special group in all the types of cancer, since they do not have special treatment protocols as children and adults have. In general, they have a worse prognosis compared with children and they can be treated in pediatric or adult oncology centers. We must therefore give special attention to this group, by conducting more studies to understand its peculiarities and to find the best treatment.

## References

1. Desandes E, Lacour B, Sommelet D, Danzon A, Delafosse P, Grosclaude P et al. Cancer survival among adolescents in France. *European Journal of Cancer*. 2006;42(3):403-409.
2. Lacour B, Goujon S, Guissou S, Guyot-Goubin A, Desmée S, Désandes E et al. Childhood cancer survival in France, 2000–2008. *European Journal of Cancer Prevention*. 2014;23(5):449-457.
3. Bleyer A, Ferrari A, Whelan J, Barr R. Global assessment of cancer incidence and survival in adolescents and young adults. *Pediatric Blood & Cancer*. 2017;64(9):e26497.
4. Lantigua C. Nathan and Oski's hematology of infancy and childhood. Philadelphia (Pa.): Saunders Elsevier; 2009.

# Assessment of risk of anesthesia in the early childhood period

**Source:** Vutskits L, Davidson A. Update on developmental anesthesia neurotoxicity. *Curr Opin Anaesthesiol.* 2017 Jun;30(3):337-342.

**T**his study presents a review of a topic that is gaining prominence in the pediatric area. It discusses the possible alteration and impairment of neuropsychomotor development in children secondary early life exposure to general anesthesia.

Initially the authors addressed the neurotoxicity of anesthesia in experimental studies in primates exposed to anesthesia in early life. Raper et al<sup>1</sup> carried out the first study in which exposed Rhesus monkeys 6-10 days of age to anesthesia with sevoflurane, and repeat the exposure 14 and 28 days after. When evaluated at 6 months, the exposed monkeys exhibited elevated anxiety compared to the control group.

In a second experiment, the motor consequences and long-term behavior were evaluated, with impact in both areas. Research has also been carried out on rodents showing changes in neurological and cognitive development<sup>2</sup>.

Using electron microscope analysis of hippocampal tissue from adult rats receiving sevoflurane anesthesia in the early neonatal period Amrock et al<sup>3</sup> found that a single exposure may reduce synaptic density and repeated exposure led to greater synaptic loss.

## Human studies

Until very recently, most of the studies were retrospective cohorts, through an outcome, such as school performance, or neurodevelopmental dysfunction and learning difficulties, therefore was researched the exposure to anesthesia in the early life period. Little evidence was found in association.

In the current studies with psychometric tests, deficits of language, cognition, memory and oral comprehension were found.

The problem of cohort studies is concerned to their confounding factors. Children who underwent anesthesia in general have or had other risk factors that may already cause problems in neurodevelopment<sup>8</sup>. Another factor discussed would be the stress that the surgery alone would cause.

More recently the pediatric anesthesia neurodevelopment assessment (PANDA) obtained the most robust study of published cohorts. It was performed in 4 American hospitals. A total of 105 children aged 8 to 15 years were identified to had hernia repair before 3 years and were matched with children of similar age without repair. Psychometric tests were performed and the comparison of IQ was the first outcome<sup>4</sup>.



The full scale IQ was 111 in both groups with difference between exposed and non-exposed of 0.2 points (95% confidence interval - 2.6 to 2.9). Evaluating subdomains were 0.5 (95% CI - 2.7 to 3.7) in IQ performance, and 0.5 (95% CI -3.2 to 2.2) in verbal IQ. In general there was no significant difference between groups. And in other tests as memory, learning, motor, speed of processing, language, attention, executive function and visuospatial skills, there were no difference. Sub-analyses were also performed between patients who had 120 and 80 minutes of anesthesia, with no difference in outcome, and the age of exposure was compared with no change in outcome also.

Two similar Canadian studies examined association between surgery in young children and later performance in the Early Development Index (EDI). EDI is a readiness school test applied at 5 years, covering 5 domains (physical health and wellbeing, knowledge and social competence, emotional health and maturity, language development and cognitive).

In the Ontario study 28366 children with surgeries before EDI were matched, and mainly showed differences with same age peers regarding physical health and well-being, as well as social knowledge and competence domains. In sub-evaluations it was only possible to perceive a difference in anaesthetized children aged 2-4 years<sup>5</sup>.

The study of Manitoba was compared in the areas of communication and domains of general knowledge, language and cognitive development. They compared 33514 children who received anesthesia before the age of 4 years with the control group. The primary outcome is grade level at 16 years and the second IQ. As in the other study, there was evidence of little variation, from 0.41% (95% CI 0.12 to 0.70%) lower school scores and 0.97% (95% CI 0.15 to 1.78%) lower scores on the IQ test. The impact was higher on children exposed at a later age<sup>6</sup>.

These studies were performed by anesthesiologists, but pediatricians are conducting comparative studies with anesthesia and neurodevelopment. Newton et al<sup>7</sup> reviewed children who had undergone surgery to correct tracheoesophageal fistula and found that 53% had neurodevelopmental delay, requiring interventions.

**Commentary by:** Natasha Geisel.  
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Despite the wide availability of articles on the subject, little can be said about the presence or not of impairment of neurological development secondary to the exposure of children to general anesthesia at an early age in life.

One of the high-impact articles (PANDA) did not show important differences between the exposed and non-exposed groups<sup>4</sup>. The other studies found an increase in risk but with low significance and nonspecific difference, warned of a higher risk in older children compared to infants<sup>5</sup>.

It has not been possible to prove the impact at multiple exposures when compared to single exposure, and in all articles the children were anesthetized predominantly for up to 2h<sup>4,5,6</sup>. Studies on prolonged exposure are still necessary.

We found as main biases the adverse effects of the surgery / anesthesia itself, the basic condition of the patient who needed the surgery early and even the psychological effects of the procedure<sup>8</sup>.

## References

1. Raper J, Alvarado MC, Murphy KL, Baxter MG. Multiple anesthetic exposure in infant monkeys alters emotional reactivity to an acute stressor. *Anesthesiology* 2015; 123:1084–1092.
2. Coleman K, Robertson ND, Dissen GA, et al. Isoflurane anesthesia has longterm consequences on motor and behavioral development in infant rhesus macaques. *Anesthesiology* 2017; 126:74–84.
3. Amrock LG, Starner ML, Murphy KL, BaxterMG. Long-term effects of single or multiple neonatal sevoflurane exposures on rat hippocampal ultrastructure. *Anesthesiology* 2015; 122:87–95.
4. Sun LS, Li G, Miller TL, et al. Association between a single general anesthesia exposure before age 36 months and neurocognitive outcomes in later childhood. *JAMA* 2016; 315:2312–2320.
5. O’Leary JD, Janus M, Duku E, et al. A population-based study evaluating the association between surgery in early life and child development at primary school entry. *Anesthesiology* 2016; 125:272–279.
6. Graham MR, Brownell M, Chateau DG, et al. Neurodevelopmental assessment in kindergarten in children exposed to general anesthesia before the age of 4 years: a retrospective matched cohort study. *Anesthesiology* 2016; 125:667–677.
7. Newton LE, Abdessalam SF, Raynor SC, et al. Neurodevelopmental outcomes of tracheoesophageal fistulas. *J Pediatr Surg* 2016; 51:743–747.
8. Lei SY, Hache M, Loepke AW. Clinical research into anesthetic neurotoxicity: does anesthesia cause neurological abnormalities in humans? *J Neurosurg Anesthesiol* 2014; 26:349–357.

# The influence of Pediatric Cardiopulmonary Resuscitation (CPR) Coach in the quality of CPR from resuscitation teams

**Source:** Cheng A, Duff JP, Kessler D, Tofil NM, Davidson J, Lin Y, Chatfield J, Brown LL, Hunt EA, Nye M, Gaither S, Collier H, MacKinnon L, Lowe K, Lambert V. Optimizing CPR Performance with CPR Coaching for Pediatric Cardiac Arrest: A Randomized Simulation-based Clinical Trial. *Resuscitation* (2018).

**S**urvival rates from pediatric cardiopulmonary arrest (CPA) are still poor. Despite high-quality cardiopulmonary resuscitation (CPR) improves survival and neurological outcomes, the adherence to guidelines is low. The use of CPR feedback defibrillators provides real-time feedback on rate and depth of chest compressions (CC) and measures time with and without CC. The use of these devices enhanced the quality of CPR in simulated CPA compared to the control<sup>1</sup>, but one multicenter trial showed that teams that used the visual feedback device improved their adherence to guidelines, but still had <40% compliance for chest compressions depth<sup>2</sup>. The aim of the article from Cheng et al. was to determine if integrating a trained CPR Coach within the resuscitation team in an attempt to help teams translate visual feedback from the CPR feedback defibrillator and optimize CPR delivery with CC improvement during simulated CPA. The CPR Coach also could allow the team leader to focus on advanced life support and treating reversible causes.

They conducted a prospective, multicenter, randomized controlled trial approved by Research Ethics Board, recruited participants and allocated randomly from Pediatric Intensive Care Unit and/or Emergency Departments from two American and two Canadian hospitals. Pediatric health care providers were recruited into teams of five: a team leader, an airway provider, two CPR providers (classical resuscitation team) and either a bedside provider or a CPR Coach depending on the study arm, respectively control group and intervention group.

The participants completed a demographic questionnaire and each resuscitation team participated in an 18-minute pediatric CPA scenario (i.e. hyperkalemic CPA with progression from pulseless ventricular tachycardia - ventricular fibrillation - pulseless electrical activity) with CPR quality parameters collected from a feedback defibrillator using identical pediatric manikins. All participants watched a five-minute orientation video describing how to use the CPR feedback defibrillator and the intervention group viewed an additional one-minute video describing the CPR Coach concept. CPR Coaches were trained with training video and simulation 48 hours prior to the CPA scenario in a standardized fashion by one-hour.

Coaches were instructed to point at the CPR feedback output on the defibrillator; give corrective or positive feedback as necessary; coordinate the appropriate compression: ventilation ratio prior to intubation and key tasks to reduce pause duration; remind CPR providers to deliver continuous compressions during intubation attempt or defibrillator charging.

As results, 42 teams (205 participants) were recruited in almost one year. One team was excluded from the study due to a violation of study protocol. The analyses included data from 40 teams (200 participants, 720 one-minute CPR epochs) and were performed with a significant level of 0,05. Demographic data revealed no significant differences between groups with and without CPR Coach at baseline using descriptive statistics. Independent t-tests were conducted to explore the effect of intervention between groups with and without CPR Coach.

Integrating a CPR Coach resulted in a significant improvement versus control group using confidence interval (CI) of 95% in the primary outcome of percentage of overall excellent CPR [63.3 (53.3, 73.3) vs. 31.5 (21.5, 41.5),  $p < 0.001$ ], also in the secondary outcomes: percentage of CC meeting guidelines for depth [69.5 (58.3, 80.7) vs. 38.0 (26.8, 49.2),  $p < 0.001$ ], mean compression depth [52.3 (50.2, 54.4) vs. 47.7 (45.7, 49.9),  $p < 0.001$ ], chest compression fraction (%) [81.9 (78.7, 85.1) vs. 76.5 (72.2, 80.8),  $p = 0.04$ ].

The pause durations pre-shock, peri-shock and post-shock in Resuscitation teams were shorter with CPR Coach versus control group using CI 95% with  $p < 0.05$ , just the pauses durations peri-shock exceeds 10 seconds in part of control group [9,4 (6.7,12.0)] versus CPR Coach group [5.5 (4.7,6.4)]. There was an improvement not statistically significant in percentage of CC meeting guidelines for rate in Resuscitation teams with Coach versus without Coach [88.0 (81.6, 94.4) vs. 79.5 (73.1, 85.9),  $p = 0.07$ ]. There was no significant difference between groups for mean CC rate.

**Commentary by:** Renata Carneiro da Cruz.

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The study has the merit of being one of the few that evaluates the impact of using CPR coaching in Resuscitation Teams with the use of CPR feedback defibrillator. The study had a great number of participants in the sample and showed significant improvement in CPR quality during simulated CPA in Resuscitation team with CPR Coach versus control group.

It has some limitations pointed by the authors that evaluated just one simulated CPA scenario and implementing CPR coaching in the hospitals would need human resource implications, but they suggest reallocation of existing resources.

In Brazil, CPR feedback defibrillator is available in few hospitals. The European Resuscitation Guidelines<sup>1,2</sup> mention that the effect of CPR feedback or prompt devices has been studied in two randomized trials and 11 observational studies. However just one study demonstrated a significant higher ROSC rate in patients where feedback and the methodology of this study was not clear, because feedback was activated at the discretion of the physician and there was no details of the decision-making process to activate or not the feedback. We need more studies to evaluate if the use of CPR feedback defibrillator and CPR Coaches can improve survival outcomes in CPA and also their cost-benefit.

## References

1. Raper J, Alvarado MC, Murphy KL, Baxter MG. Multiple anesthetic exposure in infant monkeys alters emotional reactivity to an acute stressor. *Anesthesiology* 2015; 123:1084–1092.
2. Coleman K, Robertson ND, Dissen GA, et al. Isoflurane anesthesia has longterm consequences on motor and behavioral development in infant rhesus macaques. *Anesthesiology* 2017; 126:74–84.