



# Glial Fibrillary Acidic Protein: Diagnostic and Prognostic Role in Psychomotor Development Dynamics in Patients with Congenital Heart Defects after Cardiovascular Surgery

Lacramioara Eliza Chiperi<sup>1,2</sup>, Adina Hutanu<sup>3,4</sup>

<sup>1</sup>Clinic of Pediatric Cardiology, Emergency Institute for Cardiovascular Diseases and Heart Transplant, Targu Mures, Romania

<sup>2</sup>George Emil Palade University of Medicine, Pharmacy, Sciences and Technology, Targu Mures, Romania

<sup>3</sup>Department of Laboratory Medicine, George Emil Palade University of Medicine, Pharmacy, Sciences and Technology, Targu Mures, Romania

<sup>4</sup>Laboratory of Humoral Immunology, Center for Advanced Medical and Pharmaceutical Research, George Emil Palade University of Medicine, Pharmacy, Sciences and Technology, Targu Mures, Romania

Congenital heart defects (CHDs) are the most common congenital malformations in pediatric pathology. Psychomotor development is impaired in 10-50% of the patients with CHD.<sup>1</sup> Several biomolecules are used as diagnostic or prognostic markers for impaired psychomotor development; however, neuromarkers have been the most efficient. Our study aimed to evaluate serum glial acidic fibrillary protein (GFAP) as a predictor of impaired early psychomotor development (in the first postoperative year) in patients with CHD who had cardiac surgery.

This was a prospective, controlled study, including 80 pediatric patients (< 6 years of age) with CHD, who needed elective surgical intervention. Each patient was evaluated using the Denver Developmental Screening Test II (DDST II) scale before surgery and 4-6 months after surgery. DDST II includes 125 items grouped into four categories: fine-motor adaptive function, gross motor function, personal-social behavior, and language. GFAP levels were checked preoperatively: 1) in the operating room after induction of anesthesia, but before starting cardiopulmonary bypass, and 2) 24 h after surgery.

GFAP value was significantly higher ( $p = 0.0046$ ) during the postoperative phase than the preoperative phase. Significant correlations between GFAP and neurodevelopmental scores were obtained in two domains: personal-social behavior and fine motor function. To establish the role of GFAP as a marker of brain development, receiver operating characteristic analysis was conducted and a good area under the curve of 0.75 was obtained (Figure 1). The analysis yielded a cut-off of 0.688.

GFAP constitutes the cytoskeleton of astrocytes. GFAP is present in the central nervous system but reaches the serum upon astrocyte injury or death. Therefore, it is used as a neuromarker for brain injury. In studies on children who had cardiovascular surgery, a significant increase in serum GFAP was observed after surgical intervention; moreover, GFAP levels correlated with factors that induce neurologic risk, including total by-pass time, aortic cross clamping time, and low temperature.<sup>2</sup> In our study, correlations between these risk factors and GFAP levels or neurodevelopmental scores were not found.

Studies on neurodevelopmental dynamics have reported contrasting results. In a study by Sanchez-de-Toledo including 39 patients, no significant difference was found in serum GFAP in the immediate postoperative period between children with normal and abnormal neurodevelopment.<sup>3</sup> A study by Graham on 97 patients showed that lower neurodevelopmental scores in early childhood are associated with higher levels of serum GFAP during surgery in neonates.<sup>4</sup> Vedovelli et al.<sup>5</sup> reported that GFAP could predict deficits in communication skills of infants and children. Vergine suggested that cardiopulmonary by-pass due to body temperature changes leads to nervous system injury, and high GFAP levels during surgery correlate with delays in psychomotor scores after 4-8 years.<sup>6</sup> They demonstrated that GFAP > 0.49 ng/ml is an important risk factor for poor neurologic function in the long-term. In our study, a cut-off value of 0.68 ng/ml was associated with neurodevelopmental delay in the short-term, that is, 4-6 months after surgery.



**Corresponding author:** Lacramioara Eliza Chiperi, Clinic of Pediatric Cardiology, Emergency Institute for Cardiovascular Diseases and Heart Transplant, Targu Mures, Romania

**e-mail:** lacramioara-eliza.pop@umfst.ro

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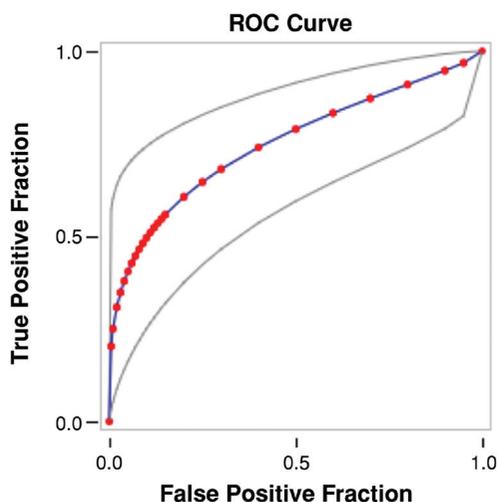
**ORCID iDs of the authors:** L.E.C. 0000-0003-3221-4276; A.H. 0000-0001-9798-1594.

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According to studies, GFAP is as good neuromarker for identifying early acute nervous system injury and long-term psychomotor impairment.<sup>7</sup>

In conclusion, we demonstrated that GFAP > 0.68 ng/ml is associated with impairment in neurodevelopmental scores of children with CHD requiring cardiovascular surgery. GFAP can serve as a good marker for short-term neurodevelopmental impairment. In addition, GFAP can prognose neurological outcomes long after the neurological insult. This neuromarker should be used in protocols for neuroprotective perioperative strategies to decrease neurological injury in patients with CHD after cardiovascular surgery.



**FIG. 1.** Receiver operating characteristic (ROC) curve for glial fibrillary acidic protein (red symbols and blue line represent a fitted ROC curve). Gray lines represent 95% confidence interval of the fitted ROC curve.

**Informed Consent:** Written informed consent was obtained from parents or guardians of children before inclusion in the study.

**Authorship Contributions:** Concept- L.E.C., A.H.; Data Collection and Processing- L.E.C., A.H.; Analysis or Interpretation- L.E.C., A.H.; Literature Search- L.E.C., A.H.; Writing- LEC

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## REFERENCES

1. Wu W, He J, Shao X. Incidence and mortality trend of congenital heart disease at the global, regional, and national level, 1990-2017. *Medicine (Baltimore)*. 2020;99:e20593. [\[CrossRef\]](#)
2. Brunetti MA, Jennings JM, Easley RB, et al. Glial fibrillary acidic protein in children with congenital heart disease undergoing cardiopulmonary bypass. *Cardiol Young*. 2013;11:1-9. [\[CrossRef\]](#)
3. Sanchez-de-Toledo J, Chrysostomou C, Munoz R, et al. Cerebral regional oxygen saturation and serum neuromarkers for the prediction of adverse neurologic outcome in pediatric cardiac surgery. *Neurocrit Care*. 2014;21:133-139. [\[CrossRef\]](#)
4. Graham EM, Martin RH, Atz AM, et al. Association of intraoperative circulating-brain injury biomarker and neurodevelopmental outcomes at 1 year among neonates who have undergone cardiac surgery. *J Thorac Cardiovasc Surg*. 2019;157:1996-2002. [\[CrossRef\]](#)
5. Vedovelli L, Padalino M, Suppiej A, et al. Cardiopulmonary-Bypass Glial Fibrillary Acidic Protein Correlates With Neurocognitive Skills. *Ann Thorac Surg*. 2018;106:792-798. [\[CrossRef\]](#)
6. Vergine M, Vedovelli L, Simonato M, et al. Perioperative Glial Fibrillary Acidic Protein Is Associated with Long-Term Neurodevelopment Outcome of Infants with Congenital Heart Disease. *Children (Basel)*. 2021;8:655. [\[CrossRef\]](#)
7. Chiperi LE, Tecar C, Toganel R. Neuromarkers which can predict neurodevelopmental impairment among children with congenital heart defects after cardiac surgery: A systematic literature review. *Dev Neurorehabil*. 2023;26:206-215. [\[CrossRef\]](#)