AEPC-YIA Session

2025年7月10日(木) 13:50 ~ 14:50 第2会場（文化会館棟 1F 中ホール）

AEPC-YIA Session（I-AEPCYIA）

Chair:Hiroyuki Yamagishi（Tokyo Metropolitan Children's Medical Center）
Chair:Nico Blom（Center for Congenital Heart Disease Amsterdam-Leiden, Leiden University Medical Center, Leiden / Amsterdam University Medical Center, Amsterdam, The Netherlands）

[I-AEPCYIA-1]

Medical and Social Outcomes of Pediatric Heart Transplantation

○Yuka Hayashida, Hidekazu Ishida, Jun Narita, Ryo Ishii, Atsuko Kato, Masaki Hirose, Yuri Suehiro, Tatsuya Baba, Yasuji Kitabatake (Department of Pediatrics, Osaka University Graduate School of Medicine, Osaka, Japan)

[I-AEPCYIA-2]

Usefulness of Fetal Electrocardiogram Monitoring in Evaluating Treatment Indications for Fetal Supraventricular Tachycardia

○Takeshi Ikegawa[1], Motoyoshi Kawataki[2], Yuki Okada[3], Yuki Kamihara[3], Michi Kasai[3], Hiromi Nagase[3], Hiroshi Ishikawa[3], Hideaki Ueda[1], Yoshitaka Kimura[4] (1.Department of Cardiology, Kanagawa Children’s Medical Center, Kanagawa, Japan, 2.Department of Neonatology, Kanagawa Children’s Medical Center, Kanagawa, Japan, 3.Department of Obstetrics, Kanagawa Children’s Medical Center, Kanagawa, Japan, 4.Department of Obstetrics and Gynecology, Tohoku University Graduate School of Medicine, Miyagi, Japan & Department of Obstetrics and Gynecology, South Miyagi Medical Center, Miyagi, Japan)

[I-AEPCYIA-3]

Enhancing Mesenchymal Stem Cells with a Mitochondria-Targeted Drug Delivery System for Cardiac Disease Treatment

○Yuji Maruo[1], Masahiro Shiraishi[2], Mitsue Hibino[3], Daisuke Sasaki[2], Jiro Abe[2], Atsuhito Takeda[2], Yuma Yamada[4] (1.Department of Pediatrics, Graduate School of Medicine, Hokkaido University, Sapporo, Japan, 2.Faculty of Pharmaceutical Science, Hokkaido University, Japan, 3.Faculty of Pharmaceutical Science, Hokkaido University ; Japan Science and Technology Agency (JST) Fusion Oriented Research for Disruptive Science and Technology (FOREST) Program)

[I-AEPCYIA-4]

Risk Factors for Reintervention in Children with Subaortic Stenosis: A 20-Year Single-Center Experience

Alessandra Zanfardino[1],○ Jelena Hubrechts[2], Alain Poncelet[1] (1.Department of Cardiovascular and Thoracic Surgery, University Hospital Saint-Luc, Université Catholique de Louvain, Brussels, Belgium, 2.Division of Congenital and Pediatric Cardiology, Department of Pediatrics, University Hospital Saint-Luc, Université Catholique de Louvain, Brussels, Belgium)

[I-AEPCYIA-5]

Genetic Background of Patients with Childhood-Onset Cardiomyopathy: Results from a Retrospective Cohort Study

○Wannes Renders[1], Evelien Cansse[1], Max Basciali[2], Joseph Panzer[1], Hans De Wilde[1], Kristof Van De Kerckhove[1], Bert Callewaert[3], Arnaud Van Lander[1], Katya De Groote[1], Daniel De Wolf[1], Laura Muiño Mosquera[1] (1.Department of pediatrics, Ghent University Hospital Ghent Belgium, 2.Faculty of medicine and health sciences, Ghent University Ghent Belgium, 3.Center for Medical Genetics, Ghent University Hospital, Ghent, Belgium)

[I-AEPCYIA-6]

Brain-Derived Neurotrophic Factor A Promising Neuromarker for Psychomotor Developmental Impairment in Children with Unrepaired Congenital Heart Defect

○Lacramioara Eliza Chiperi[1], Asmaa Carla Hagau[2], Cristina Tecar[3], Adina Hutanu[4], Iolanda Muntean[5] (1.Department of Pediatric Cardiology, Emergency Institute for Cardiovascular Diseases and Heart Transplant, Targu Mures, Romania, 2.Doctoral School of George Emil Palade University of Medicine, Pharmacy, Sciences and Technology of Targu Mures, Romania, 3.Department of Neurosciences, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania, 4.Department of Laboratory Medicine & Laboratory of Humoral Immunology, Center for Advanced Medical and Pharmaceutical Research, George Emil Palade University of Medicine, Pharmacy, Sciences and Technology of Targu Mures, Romania, 5.Clinic of Pediatric Cardiology, Emergency Institute for Cardiovascular Diseases and Transplantation of Targu Mureș, University of Medicine, Pharmacy, Sciences and Technology "George Emil Palade" of Targu Mures, 540142 Targu Mureș, Romania)

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[I-AEPCYIA-1] Medical and Social Outcomes of Pediatric Heart Transplantation

○Yuka Hayashida, Hidekazu Ishida, Jun Narita, Ryo Ishii, Atsuko Kato, Masaki Hirose, Yuri Suehiro, Tatsuya Baba, Yasuji Kitabatake (Department of Pediatrics, Osaka University Graduate School of Medicine, Osaka, Japan)

キーワード：transplantation、outcome、survival

INTRODUCTION:Advancements in immunosuppressive therapy have improved the overall survival rate of pediatric heart transplant recipients. However, the current status of social reintegration among these patients remains unclear. Research on the social outcome is further complicated by cross-national differences in educational systems and labor laws, emphasizing the importance of country-specific studies.
METHODS:This retrospective study examined 74 patients who underwent heart transplantation under 18 years of age between 2000 and 2023, and were followed-up at Osaka University Hospital, Japan. Survival rates, pre- and post-transplant complications, and educational or occupational status were analyzed.
RESULTS:The cohort consisted of 34 males and 40 females, with a median age at transplantation of 6 years (interquartile range, IQR: 2–13). The median follow-up duration was 7 years (IQR: 5–13). Twelve deaths occurred during the observation period, with 5-year, 10-year, and 15-year survival rates of 91%, 91%, and 81%, respectively. Major post-transplant complications, including allograft rejection (14 cases, 19%), post-transplant lymphoproliferative disease (13 cases, 18%), kidney dysfunction (8 cases, 11%), and coronary artery vasculopathy (5 cases, 7%) were identified during the observational period. Excluding six patients who did not reach to school age, stable school attendance was achieved in 66 out of 68 patients (97%). Among the 39 patients aged 18 years or older, 15 (38%) were employed, 14 (36%) were enrolled in higher education, and 10 (26%) were neither employed nor enrolled in education. Univariate analysis revealed that pre-transplant cerebrovascular or neurodevelopmental disorders significantly hindered educational and occupational outcomes (P = 0.0018).
CONCLUSIONS:The mortality of pediatric heart transplantation in our hospital was better than international registry data. While educational outcomes in compulsory schools were favorable among pediatric heart transplant recipients in Japan, 26% of patients above age 18 were neither employed nor enrolled in education. Neurological complications emerged as a key risk factor for social reintegration.

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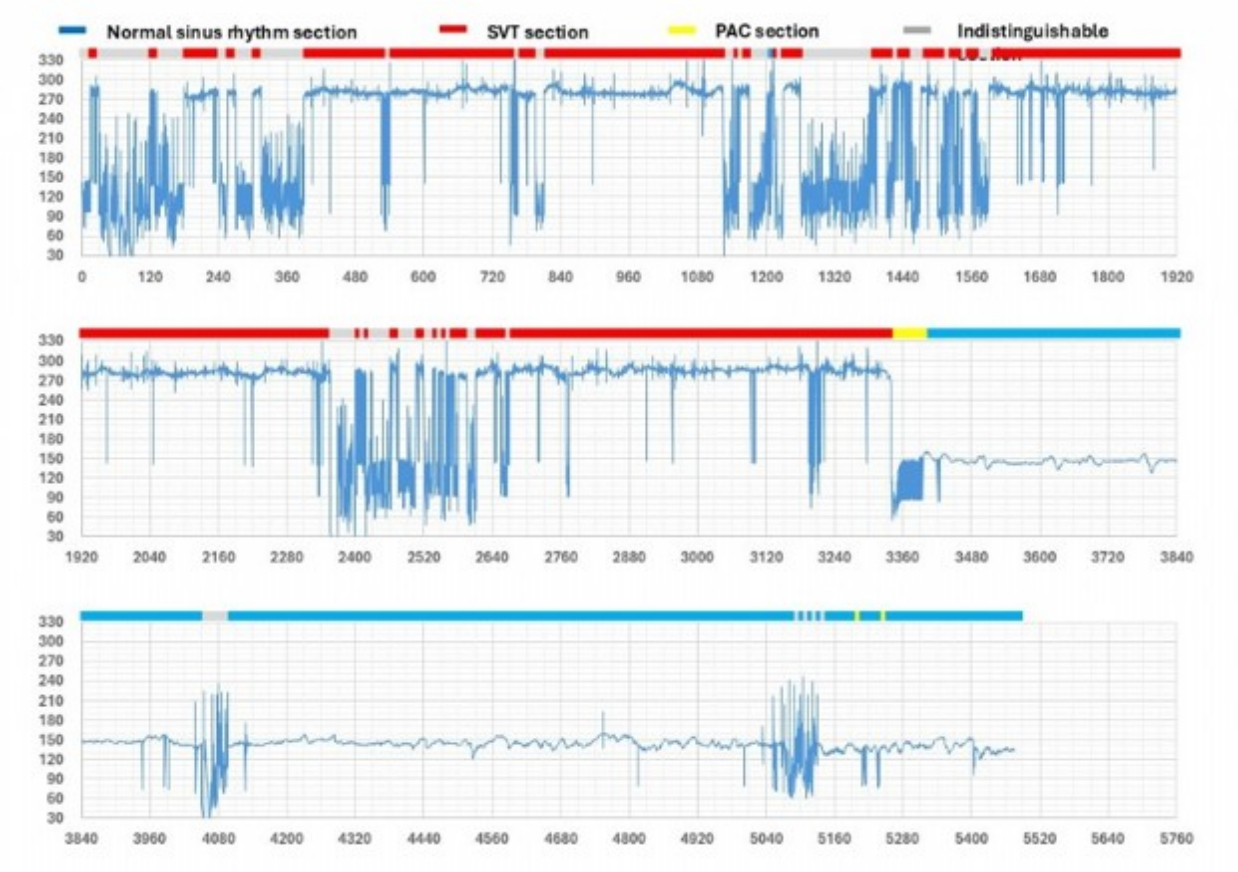
[I-AEPCYIA-2] Usefulness of Fetal Electrocardiogram Monitoring in Evaluating Treatment Indications for Fetal Supraventricular Tachycardia

○Takeshi Ikegawa[1], Motoyoshi Kawataki[2], Yuki Okada[3], Yuki Kamihara[3], Michi Kasai[3], Hiromi Nagase[3], Hiroshi Ishikawa[3], Hideaki Ueda[1], Yoshitaka Kimura[4] (1.Department of Cardiology, Kanagawa Children's Medical Center, Kanagawa, Japan, 2.Department of Neonatology, Kanagawa Children's Medical Center, Kanagawa, Japan, 3.Department of Obstetrics, Kanagawa Children's Medical Center, Kanagawa, Japan, 4.Department of Obstetrics and Gynecology, Tohoku University Graduate School of Medicine, Miyagi, Japan & Department of Obstetrics and Gynecology, South Miyagi Medical Center, Miyagi, Japan)
キーワード：fetus、electrocardiogram、supraventricular tachycardia

INTRODUCTION:Approximately 41% of fetal supraventricular tachycardia (SVT) cases progress to fetal hydrops, especially when tachycardia is present for >50% of the monitoring time, necessitating consideration of transplacental therapy with antiarrhythmic drugs. Current methods for assessing fetal heart rate, such as delivery monitoring devices, rely on Doppler ultrasound and may fail to accurately count heart rates during extrasystoles or significant tachycardia.
METHODS:We report a case of fetal SVT caused by premature atrial contraction with block, which could not be evaluated via fetal heart rate monitoring using a delivery monitor.
RESULTS:The patient was a 37-year-old woman at 28 weeks' gestation referred for fetal tachycardia detected during routine examination. Fetal echocardiography (ECG) revealed occasional premature atrial contractions (PAC) with block and SVT, with heart rates of approximately 270 beats per minute during SVT. Despite normal thyroid function and autoimmune disease tests, fetal echocardiography could not consistently assess the frequency of arrhythmias due to the fluctuating nature of the SVT episodes. To improve assessment, fetal ECG monitoring was employed at 29 and 31 weeks gestation. The prolonged ECG allowed for a more accurate measurement of tachycardia frequency. The fetal ECG revealed that SVT accounted for less than 50% of the monitoring time (Figure 1). By 31 weeks, the frequency of SVT was low enough to avoid immediate therapeutic intervention. The mother was discharged at 31 weeks and monitored outpatient, with no further signs of fetal hydrops. She delivered a healthy baby boy at 38 weeks without arrhythmias or cardiac abnormalities.
CONCLUSIONS:The findings suggest that prolonged fetal ECG monitoring is a valuable tool in evaluating the frequency of fetal arrhythmias, offering a less invasive and more accurate alternative to traditional methods, such as Doppler ultrasound and fetal echocardiography. This approach is particularly useful in cases of intermittent tachyarrhythmias where precise frequency data are critical for determining the need for treatment. In this case, prolonged fetal electrocardiogram monitoring was useful in

determining the need for fetal therapy.

Figure 1
Analysis and summary of the second fetal echocardiography (ECG) monitoring on the same day at 31 weeks' gestation. The figure shows the change over time in the fetal heart rate (blue line) obtained from the fetal electrocardiogram. The vertical axis represents the heart rate (bpm), and the horizontal axis represents the elapsed time (s). The normal sinus rhythm section is shown in light blue, supraventricular tachycardia (SVT) section in red, premature atrial contraction (PAC) section in yellow, and indistinguishable section due to unclear fetal bioelectrical signals in gray. SVT is 47.7% and does not exceed 50%.



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[I-AEPCYIA-3] Enhancing Mesenchymal Stem Cells with a Mitochondria-Targeted Drug Delivery System for Cardiac Disease Treatment

○Yuji Maruo[1], Masahiro Shiraishi[2], Mitsue Hibino[3], Daisuke Sasaki[2], Jiro Abe[2], Atsuhito Takeda[2], Yuma Yamada[4] (1.Department of Pediatrics, Graduate School of Medicine, Hokkaido University, Sapporo, Japan, 2.Faculty of Pharmaceutical Science, Hokkaido University, Japan, 3.Faculty of Pharmaceutical Science, Hokkaido University ; Japan Science and Technology Agency (JST) Fusion Oriented Research for Disruptive Science and Technology (FOREST) Program)
キーワード：Mesenchymal stem cell、Coenzyme Q10、Drug delivery system

INTRODUCTION:We successfully developed mitochondria-activated cardiac-derived cells (MITO cells) by introducing mitochondrial functional molecules, such as resveratrol and coenzyme Q10 (CoQ10), into cardiac-derived cell mitochondria using the MITO-Porter system, a mitochondria-targeted drug delivery system. Previous studies demonstrated that transplantation of MITO cell in doxorubicin-induced cardiomyopathy model mice and myocardial ischemia-reperfusion injury model mice and rats exhibited superior preventive and therapeutic effects compared to conventional cell transplantation therapy. However, for clinical applications, it is necessary to identify transplantable stem cells that can be mass-produced and offer greater versatility. To address this issue, we focused on mesenchymal stem cells (MSCs), which are progressing toward clinical use. The efficacy of MSC transplantation therapy has been reported in various diseases, including cardiac conditions. The objective of this study was to validate whether treatment with CoQ10 encapsulated within the MITO-Porter system enhances mitochondrial functions in MSCs, thereby improving the potential efficacy of MSC transplantation therapy.
METHODS:In this study, we used highly purified human bone marrow-derived mesenchymal stem cells, referred to as rapidly expanding clones (RECs). We treated RECs with CoQ10 encapsulated within the MITO-Porter system, and their cellular uptake was evaluated by flow cytometry. We assessed intracellular localization using confocal laser scanning microscopy, while changes in mitochondrial respiratory capacity were evaluated using an extracellular flux analyzer.
RESULTS:Flow cytometry revealed that cellular uptake of CoQ10 encapsulated within the MITO-Porter was significantly increased compared to the non-treatment group. Confocal laser scanning microscopy demonstrated co-localization of fluorescent signals, with yellow signals indicating overlap between mitochondria labeled with a red fluorophore and the MITO-Porter labeled with a green fluorophore. Treatment with CoQ10 encapsulated within the MITO-Porter significantly enhanced mitochondrial respiratory capacity as measured by the extracellular flux analyzer.
CONCLUSIONS:Treatment with CoQ10 encapsulated within the MITO-Porter system

effectively enhanced the mitochondrial respiratory capacity in MSCs. The MITO-Porter system represents a promising approach to improve MSC transplantation therapy. Future studies will focus on evaluating the therapeutic efficacy of mitochondria-activated MSCs in cardiac diseases models through in vivo experiments.

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[I-AEPCYIA-4] Risk Factors for Reintervention in Children with Subaortic Stenosis: A 20-Year Single-Center Experience

Alessandra Zanfardino[1],○ Jelena Hubrechts[2], Alain Poncelet[1] (1.Department of Cardiovascular and Thoracic Surgery, University Hospital Saint-Luc, Université Catholique de Louvain, Brussels, Belgium, 2.Division of Congenital and Pediatric Cardiology, Department of Pediatrics, University Hospital Saint-Luc, Université Catholique de Louvain, Brussels, Belgium)
キーワード：subaortic stenosis、recurrence risk、surgical resection

INTRODUCTION:Subaortic stenosis (SAS) is a lesion of the left ventricular outflow tract found in 2-6% of children with congenital heart defects. Despite good short-term surgical outcomes, recurrences are not rare, with reintervention required in up to 30%. The mechanisms behind lesion recurrence remain unclear. Tunnel-like lesions, higher preoperative peak gradients, and younger age at surgery have been associated with increased recurrence risk. Our study aimed at identifying risk factors for reintervention in children with recurrent SAS following a first successful resection.
METHODS:This retrospective study included 76 pediatric patients treated for SAS at University Hospital Saint-Luc (Brussels) from 2000 to 2020. Data from ultrasounds, clinical records and surgeries were analysed, considering patients' age, weight, height at surgery, type of SAS, associated cardiac malformations and concomitant myomectomy. Statistical analysis was conducted using IBM SPSS software to identify predictors of recurrence.
RESULTS:The median age at surgery was 3 years (IQR 25-75: 1.6-5.6 years), with a male predominance (60.5%). Nearly 80% of patients had associated cardiac malformations. After several years of follow-up, the recurrence rate was 13.1%. Younger age, smaller size, and a lesion-to-valve distance of 8 mm or more, particularly in fibromuscular or tunnel-like lesions, were correlated to higher reintervention risk. The 10-year reintervention-free survival rate was 89.5%.
CONCLUSIONS:Managing SAS in children remains challenging due to the significant risk of recurrence. The study identified key predictors of reintervention, stressing the importance of individualised treatment plans and close monitoring, especially for younger patients with specific anatomical abnormalities, to improve long-term outcomes.

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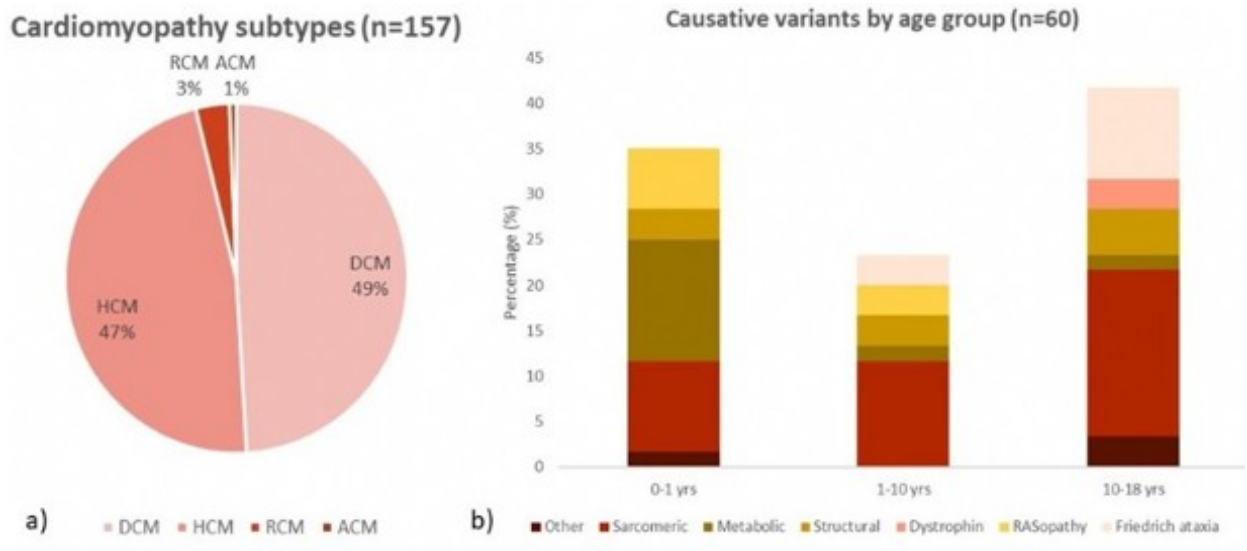
[I-AEPCYIA-5] Genetic Background of Patients with Childhood-Onset Cardiomyopathy: Results from a Retrospective Cohort Study

○Wannes Renders[1], Evelien Cansse[1], Max Basciali[2], Joseph Panzer[1], Hans De Wilde[1], Kristof Van De Kerckhove[1], Bert Callewaert[3], Arnaud Van Lander[1], Katya De Groote[1], Daniel De Wolf[1], Laura Muiño Mosquera[1] (1.Department of pediatrics, Ghent University Hospital Ghent Belgium, 2.Faculty of medicine and health sciences, Ghent University Ghent Belgium, 3.Center for Medical Genetics, Ghent University Hospital, Ghent, Belgium)
キーワード：Genetics、Childhood-onset cardiomyopathy、sarcomere genes

INTRODUCTION:Childhood-onset cardiomyopathy (CMP) has a rare incidence of approximately 1/100 000 children. 40-50% of children have a positive familial history of cardiomyopathy or sudden cardiac death and the general yielding across the different types of CMP is 50-60%, with dilated CMP (DCM) having the lowest genetic yield (20-30%). A high proportion of rare disease phenocopies such as metabolic disorders and RASopathies is generally found in early childhood (<10yrs).
AIM: To investigate genotype-phenotype correlations and cardiac outcomes.
METHODS:Children under 18yrs who presented at our institution between 1990-2024 with any type of CMP, were included in the study. Demographic, genetic, and cardiac outcome data were collected and analyzed.
RESULTS:A total of 157 children (63.1% male, mean age: 5.3±5.8yrs) were diagnosed with CMP. The most frequent subtypes were DCM (49%) and hypertrophic CMP (HCM, 47.1%) with fewer cases of restrictive CMP (RCM, 5 patients) and arrhythmogenic CMP (ACM, 1 patient). Nearly half of the patients (46.5%) were diagnosed during infancy. Genetic screening was performed in 68.8% of patients, most frequently in HCM (74.3%). Overall, a causative variant was identified in 56.5%. Genetic yield was higher in children with HCM in comparison to those with DCM (65.4% vs 46.9%, p=0.067). Additionally, in 15.7% variants of unknown significance (VUS) were found. A trend of higher genetic yield was seen in older age groups. In infants (0-1yrs), a variant in a metabolic or RASopathy gene was found in 57.1%. Notably, sarcomere gene variants, traditionally associated with adult-onset CMP, contributed to 28.6% of infant cases. Major cardiac events occurred in 43.3%. Of all patients 25.5% died, 12.1% underwent a heart transplant and 7% received an implantable cardioverter-defibrillator. No significant differences in outcomes were observed across CMP subtypes.
CONCLUSIONS:Genetic testing identified the underlying etiology in over 50% of patients with childhood-onset CMP. While rare disease phenocopies are highly prevalent in infants, sarcomere gene variants –once thought to be limited to adult-onset CMP– can also manifest in a very young age. These findings underscore the importance of early genetic testing to guide diagnosis and management.

Figure 1. a) Distribution of cardiomyopathy subtypes. DCM= Dilated CMP, HCM = Hypertrophic CMP, RCM = Restrictive CMP, ACM = Arrhythmogenic CMP b) Causative variants (likely pathogenic and pathogenic) per gene category, displayed according to age group. In the "structural" group genes encoding the Z-disc (ACTN2, NEXN2), nuclear envelope (LMNA), cytoskeletal (FLNC, DES) and junctional membrane (JPH2) are included.



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[I-AEPCYIA-6] Brain-Derived Neurotrophic Factor A Promising Neuromarker for Psychomotor Developmental Impairment in Children with Unrepaired Congenital Heart Defect

○Lacramioara Eliza Chiperi[1], Asmaa Carla Hagau[2], Cristina Tecar[3], Adina Hutanu[4], Iolanda Muntean[5] (1.Department of Pediatric Cardiology, Emergency Institute for Cardiovascular Diseases and Heart Transplant, Targu Mures, Romania, 2.Doctoral School of George Emil Palade University of Medicine, Pharmacy, Sciences and Technology of Targu Mures, Romania, 3.Department of Neurosciences, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania, 4.Department of Laboratory Medicine & Laboratory of Humoral Immunology, Center for Advanced Medical and Pharmaceutical Research, George Emil Palade University of Medicine, Pharmacy, Sciences and Technology of Targu Mures, Romania, 5.Clinic of Pediatric Cardiology, Emergency Institute for Cardiovascular Diseases and Transplantation of Targu Mureș, University of Medicine, Pharmacy, Sciences and Technology "George Emil Palade" of Targu Mures, 540142 Targu Mureș, Romania)
キーワード：Psychomotor development、congenital heart defect、neuron specific enolase

INTRODUCTION:In patients with congenital heart defects (CHD), psychomotor delay is frequently detected (20-50% of cases), not only in those with cyanogenic malformations but also in those with normal cerebral tissue oxygenation (non-cyanogenic malformations). The aim of the study was to assess the predictive value of neuromarkers for psychomotor performance of CHD patients.
METHODS:This cross-sectional study included children aged 0-6 years with CHD who had not undergone treatment (interventional or cardiac surgery). Children with known factors that could affect psychomotor development such as prematurity, perinatal asphyxia or genetic syndromes, were excluded. Psychomotor development was evaluated using Denver Developmental Screening Test II (DDSTII). Blood samples were collected for neuromarkers analysis: neuron-specific enolase (NSE), protein S100 (pS100), brain-derived neurotrophic factor (BDNF) and glial fibrillary acidic protein (GFAP).
RESULTS:We enrolled 77 children who had normal development based on pediatric examination and were subsequently thoughtful evaluated through DDSTII. Patients with CHD experienced more frequent developmental delays compared to healthy children (56% in the non-cyanotic group and 97% in the cyanotic group). The association between type of CHD (cyanotic or non-cyanotic) and psychomotor impairment was statistically significant ($p<0.0001$, RR=2.604, CI=2.07-3.26).
Neuromarker values were compared between cyanotic and non-cyanotic groups: NSE and BDNF values were higher in the cyanotic group, while pS100 and GFAP values were slightly higher in the non-cyanotic group, though without statistical significance. Only BDNF showed a positive significant correlation with psychomotor development ($r=0.35$, $p=0.023$). An AUC of 0.72 was obtained for psychomotor development and BDNF in ROC

analysis, with a cut-off value of 5895 pg/ml. Multivariate analysis using a multiple logistic regression model indicated that none of the independent variables tested had a statistically significant relationship with BDNF levels.
CONCLUSIONS:Among the studied neuromarkers (NSE, pS100, BDNF, GFAP), only BDNF demonstrated moderate discriminative ability in predicting psychomotor development outcomes in pediatric patients with CHD. In this pilot study, BDNF shows promise, but further studies are needed to assess its clinical significance and potential applications.