DOI: 10.15825/1995-1191-2026-1-147-153

RISK FACTORS FOR ADVERSE OUTCOMES IN PEDIATRIC HEART TRANSPLANTATION

E.A. Spirina[1], D.V. Ryabtsev[1], V.V. Kolyadina[1], A.Ch. Chartaev[1], A.S. Epremyan[1], A.K. Solodovnikova[1], A.A. Kuznetsova[1], A.S. Ignatkina[1], N.S. Pravkina[1], Ya.S. Karina[1], S.V. Gautier[1, 2]

[1] Shumakov National Medical Research Center of Transplantology and Artificial Organs, Moscow, Russian Federation

[2] Sechenov University, Moscow, Russian Federation

Heart transplantation (HT) remains the only definitive surgical treatment for end-stage chronic heart failure (CHF). **Objective:** to investigate factors associated with adverse immediate outcomes following HT in children. **Materials and methods.** Between January 1, 2012, and December 31, 2024, 91 HTs were performed in recipients under 18 years of age at Shumakov National Medical Research Center of Transplantology and Artificial Organs, Moscow. The patients were divided into two groups based on early postoperative outcomes: survivors (n = 79; 86.8%) and non-survivors (n = 12; 13.2%). **Results.** Between 2012 and 2024, a total of 2,190 HTs were performed, including 91 (4.2%) in children. Severe early graft dysfunction occurred in 14 pediatric heart recipients (15.4%), and in-hospital mortality was 13.2%. A high recipient urgency status (UNOS), the use of short-term mechanical circulatory support, and clinical manifestations of multiple organ failure necessitated the expansion of donor heart selection criteria. Receiver operating characteristic (ROC) analysis demonstrated that baseline laboratory parameters influenced transplant outcomes. Serum sodium, lactate, and urea levels, as well as hemoglobin levels, red blood cell and platelet counts, showed statistically significant predictive value, as confirmed by area under the curve (AUC) analysis. Donors in the non-survivor group were significantly older than those in the survivor group. The donor-to-recipient weight ratio was higher among recipients who died in the early post-transplant period. In the non-survivor cohort, significantly higher values were observed for the donor-to-recipient height ratio, donor-to-recipient body surface area ratio, and durations of graft ischemia, anesthesia, surgery, and cardiopulmonary bypass. **Conclusion.** The effectiveness of pediatric HT (hospital survival rate 86.8%) is influenced primarily by recipient urgency status (UNOS). Additional contributing factors include severity of multiple organ dysfunction, donor age, significant donor–recipient anthropometric mismatch, operative time, and intraoperative blood loss.

Keywords: pediatric heart transplantation, heart donor, urgent indications for heart transplantation, risk factors.

INTRODUCTION

Heart transplantation (HT) remains the only definitive surgical treatment for patients with end-stage chronic heart failure (CHF). At present, deceased organ donation from donors younger than 18 years is not practiced in the Russian Federation; therefore, HT using hearts from adult donors is the only available treatment option for pediatric recipients requiring HT.

Numerous single-center and multicenter studies have evaluated the influence of donor- and recipient-related risk factors on HT outcomes. In recipients with a high urgency status, the necessity for urgent transplantation often requires the use of expanded criteria donors, which significantly affects the intraoperative course. Furthermore, transplantation performed in the absence of complete anthropometric compatibility or using organs from older donors may be considered in children requiring urgent surgery, although such procedures are associated with an increased risk of adverse outcomes [1].

At Shumakov National Medical Research Center of Transplantology and Artificial Organs, experience in pediatric HT accumulated between January 1, 2012, and December 31, 2024, formed the basis of the present study.

Study objective: to investigate factors adversely affecting the immediate outcomes of HT in pediatric recipients receiving donor hearts from individuals older than 18 years.

STUDY POPULATION

Between January 1, 2012, and December 31, 2024, a total of 91 orthotopic HTs were performed in recipients younger than 18 years at Shumakov National Medical Research Center of Transplantology and Artificial Organs. Among the recipients, 36 (39.6%) were girls and

Corresponding author: Ekaterina Spirina. Address: 1, Shchukinskaya str., Moscow, 123182, Russian Federation. Phone: (968) 048-35-26. E-mail: spirina.ekaterina2011@yandex.ru

55 (60.4%) were boys, aged 6 to 17 years (mean age: 13.9 ± 2.3 years). The principal causes of end-stage CHF were cardiomyopathy in 81 patients (89.0%) and congenital heart disease (CHD) in 7 patients (7.7%).

The severity of CHF according to the New York Heart Association (NYHA) classification corresponded to functional classes II–IV, with a mean functional class of 3.2 ± 0.5. In 41 (45.1%) patients, the urgency of HT were classified as United Network for Organ Sharing (UNOS) status 2, 18 patients (19.8%) as status 1B, and 32 patients (35.2%) as status 1A.

Twenty-one (23.1%) HT recipients underwent repeat cardiac surgery. In 36 (39.6%) patients, short-term (n = 26 (24.2%)), long-term (n = 8 (8.8%)), or a combination (long-term and short-term) (n = 2 (2.2%)) of mechanical circulatory support (MCS) was used prior to HT. Pre-HT venoarterial extracorporeal membrane oxygenation (VA-ECMO) lasted for 1–20 (4.50 [1.75; 6.00]) days. In 10 (11.0%) recipients, a HeartMate III left ventricular bypass (Abbott Laboratories, USA) was implanted prior to HT, with a duration of 7–1,019 (609.5 [576.25; 880.0]) days.

Heart recipients (n = 91) were divided into 2 clinical groups:

Group 1 – heart transplants in children from donors older than 18 years with a favorable outcome – surviving recipients (n = 79; 86.8%);

Group 2 – heart transplants in children from donors older than 18 years with an unfavorable outcome – deceased recipients (n = 12; 13.2%).

Statistical analysis was performed using Statistica 12 and SPSS 26. Quantitative variables are presented as the arithmetic mean and standard deviation, as well as the median and interquartile range. Differences between the two groups were assessed using Student's t-test, as well as the Mann–Whitney U-test in cases of non-normal distribution. A ROC analysis was performed to determine the predictive significance of the quantitative variables. The optimal cutoff value was determined based on the Youden index. A p-value of <0.05 was considered statistically significant.

RESULTS

Between 2012 and 2024, the Shumakov National Medical Research Center of Transplantology and Artificial Organs performed 2,190 HTs, of which 91 (4.2%) were carried out in pediatric recipients. The proportion of pediatric HTs among the total number of HTs performed annually during the study period (2012–2024) ranged from 0.98% in 2013 to 7.2% in 2024 (Fig.).

HT in children (n = 91) was performed using donor hearts obtained from individuals with confirmed brain death resulting from either non-traumatic brain injury (BI) in 58 cases (63.7%) or traumatic BI in 33 cases (36.3%). Donor age ranged from 18 to 67 years (mean age: 36.7 ± 11.7 years), while the age difference between donors and recipients ranged from 3 to 58 years (22.6 ± 12.5 years).

The median graft ischemia duration was 176.50 [137.00; 210.50] minutes, whereas cold ischemic time was 97.00 [79.00; 125.50] minutes. The maximum vasoactive–inotropic score was 11.3 [7.25; 18.23]. Median intraoperative blood loss was 800.0 [500.00; 1400.00] mL, while postoperative blood loss was 250.0 [150.00; 375.00] mL. Postoperative mechanical ventilation lasted for 10.0 [5.97; 24.25] hours. Post-transplant MCS was required in 36 recipients (39.7%) for a median duration of 3.0 [1.48; 4.50] days.

Severe early graft dysfunction developed in 14 recipients (15.4%). The overall in-hospital mortality rate was 13.2%.

The results of a comparative analysis of pre-transplant recipient characteristics, donor parameters, and intraoperative variables between surviving (n = 79; 86.8%) and deceased recipients (n = 12; 13.2%) are presented in Table 1.

Deceased patients more often required urgent HT and short-term pre-transplant MCS. In addition, these patients were generally younger and had lower anthropometric characteristics compared with surviving recipients.

Table 2 summarizes the comparative analysis of pre-transplant laboratory parameters in surviving (n = 79) and deceased (n = 12) recipients under 18 years of age.

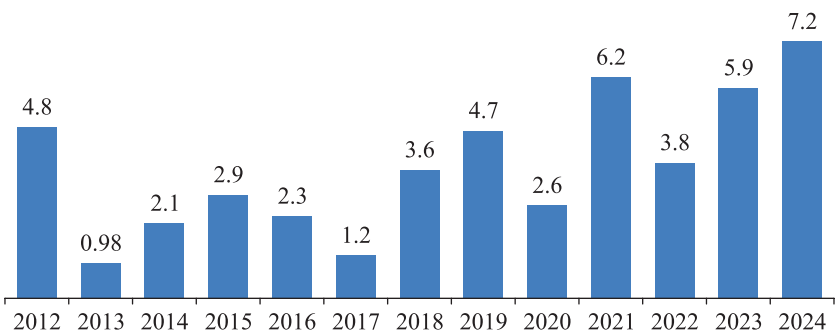

Fig. Percentage of heart transplants (HTs) performed in recipients under 18 years of age relative to the total number of HTs conducted at Shumakov National Medical Research Center of Transplantology and Artificial Organs (October 1, 2012 – December 31, 2024)

Pre-transplant hemoglobin, red blood cell, and platelet levels were significantly lower in the group of deceased recipients. These patients also demonstrated lower levels of mixed venous oxygen saturation (SvO_2) and serum sodium (Na^+) ($p < 0.005$). In this same cohort of recipients, significantly higher pre-transplant levels of

Table 1

Pre-transplant clinical characteristics of surviving and non-surviving transplant recipients in the early post-transplant period

Parameters	Heart recipients under 18 years of age		p
	Survivors (n = 79)	Deceased (n = 12)	
Age, years (mean ± SD)	14.10 ± 2.13	12.5 ± 6.9	0.023
Sex, n (%) Boys Girls	 51/64.6 28/35.4	 4/33.3 8/66.7	0.057
Weight, kg (Me [Q1; Q3])	50.0 [38.5; 65.0]	31.5 [25.25; 37.75]	<0.0001
Height, cm (Me [Q1; Q3])	163.0 [152.0; 174.0]	145.5 [131.75; 153.0]	<0.0001
BSA, m^2 (mean ± SD)	1.54 ± 0.31	1.15 ± 0.27	<0.0001
NYHA FC (Me [Q1; Q3])	3.00 [3.00; 4.00]	4.00 [3.00; 4.00]	0.158
UNOS status (Me [Q1; Q3]) 1A 1B 2	 23/29.1 15/19.0 41/51.9	 9/75.0 3/25 0/0.0	<0.030
Short-term MCS, n/% VA-ECMO Other	 17/21.5	 7/66.7 1/8.3	<0.003
Short-term MCS, days (Me [Q1; Q3])	3.60 [1.09; 5.25]	5.00 [3.82; 6.00]	0.239

Note: p – significance level. Abbreviations: SD, standard deviation; Me, median; Q1, first quartile (25th percentile); Q3, third quartile (75th percentile); BSA, body surface area; NYHA FC, New York Heart Association functional classification; MCS, mechanical circulatory support; VA-ECMO, venoarterial extracorporeal membrane oxygenation.

Table 2

Comparative analysis of pre-transplant laboratory tests in surviving (n = 79) and non-surviving (n = 12) heart transplant recipients

Parameters	Heart recipients under 18 years of age		p
	Survivors (n = 79) (Me [Q1; Q3])	Deceased (n = 12) (Me [Q1; Q3])	
Hemoglobin, g/L	125.0 [105.00; 142.00]	96.0 [81.50; 115.0]	0.018
Erythrocytes, $\times 10^9$/L	4.50 [4.11; 4.98]	3.70 [3.03; 4.23]	0.011
Platelets, $\times 10^9$/L	210.00 [162.00; 262.00]	122.00 [58.60; 219.00]	0.020
Leukocytes, $\times 10^9$/L	7.90 [6.65; 8.30]	7.60 [6.00; 7.60]	0.954
Urea, mmol/L	5.50 [4.60; 8.07]	7.9 [6.30; 12.92]	0.014
Creatinine, μmol/L	63.9 [48.66; 78.25]	48.20 [38.76; 70.75]	0.749
Total bilirubin, μmol/L	23.20 [12.91; 36.35]	46.00 [10.64; 60.03]	0.042
ALT, U/L	20.90 [16.00; 51.70]	24.50 [11.17; 68.19]	0.373
AST, U/L	29.30 [21.47; 39.70]	32.70 [26.50; 106.34]	0.250
Albumin, g/L	41.40 [24.00; 54.60]	44.40 [41.81; 45.04]	0.310
Total protein, g/L	69.00 [65.50; 74.13]	66.60 [61.15; 75.60]	0.850
NT-proBNP	2530.00 [1514.25; 6393.00]	9016.00 [6207.00; 11825.00]	0.012
pH	7.40 [7.33; 7.40]	7.40 [7.38; 7.45]	0.351
BE, mmol/L	–0.20 [–1.40; 1.98]	0.40 [–3.25; 2.35]	0.821
pO_2, mm Hg	38.50 [31.73; 44.63]	31.70 [26.40; 42.45]	0.350
SpO_2, %	67.00 [57.10; 75.30]	58.60 [39.10; 71.95]	0.005
Lactate, mmol/L	1.00 [0.90; 1.40]	1.54 [1.35; 2.95]	0.001
Na^+, mmol/L	139.0 [137.0; 140.0]	135.0 [134.0; 138.0]	0.009
K^+, mmol/L	3.50 [3.33; 3.88]	4.0 [3.50; 4.25]	0.042

Abbreviation: ALT, alanine aminotransferase; AST, aspartate aminotransferase; NT-proBNP, N-terminal pro–B-type natriuretic peptide; BE, base excess.

urea, total bilirubin, and N-terminal pro–B-type natriuretic peptide (NT-proBNP) were observed.

Receiver operating characteristic (ROC) analysis further confirmed the prognostic significance of baseline laboratory parameters for HT outcomes (Table 3). Table 4 presents the threshold values of parameters associated with an increased risk of mortality.

The high urgency status (UNOS classification), the requirement for short-term MCS, and clinical manifestations of multiple organ failure in recipients necessitated expansion of the criteria for donor heart utilization.

Table 5 presents the results of the comparative analysis of donor heart characteristics between recipients who survived and those who died during the early post-transplant period.

Heart donors in the cohort of deceased recipients were significantly older than donors in the cohort of survivors.

Among recipients who died in the early post-transplant period, the donor-to-recipient weight ratio was higher, as were the donor-to-recipient height ratio and the donor-to-recipient body surface area ratio, compared with surviving recipients.

Table 6 presents the comparative analysis of intraoperative characteristics between recipients who survived and those who died during the early post-transplant period.

Table 3

ROC analysis: AUC and 95% CI for pre-transplant laboratory parameters in heart transplant recipients under 18 years of age

Indicator	AUC (95% CI)	p (AUC)
Na^+, mmol/L	0.761 (0.597–0.925)	0.002
Erythrocytes, $\times 10^9$/L	0.742 (0.567–0.918)	0.007
Hemoglobin, g/L	0.738 (0.567–0.909)	0.006
Lactate, mmol/L	0.737 (0.572–0.903)	0.005
Urea, mmol/L	0.722 (0.562–0.883)	0.007
Platelets, $\times 10^9$/L	0.692 (0.514–0.869)	0.034
SpO_2, %	0.622 (0.406–0.838)	0.27
Total bilirubin, μmol/L	0.577 (0.341–0.813)	0.522
NT-proBNP	0.825 (0.617–1.000)	0.002

Table 4

Optimal threshold values and diagnostic threshold characteristics in heart transplant recipients under 18 years of age, including sensitivity (Se), specificity (Sp), positive predictive value (PPV), and negative predictive value (NPV)

Indicator	Threshold (Youden's J statistic)	Se	Sp	PPV	NPV
Na^+, mmol/L	≥139	0.636	0.838	0.368	0.939
Red blood cells, $\times 10^9$/L	≤3.8	0.636	0.827	0.35	0.939
Hemoglobin, g/L	≤97	0.636	0.813	0.333	0.938
Lactate, mmol/L	≥1.3	0.818	0.703	0.29	0.963
Urea, mmol/L	≥6.6	0.727	0.68	0.25	0.944
Platelets, $\times 10^9$/L	≤122	0.818	0.68	0.273	0.962
SpO_2, %	≤39.8	0.364	0.959	0.571	0.91
Total bilirubin, μmol/L	≥46	0.545	0.827	0.316	0.925
NT-proBNP	≥3,398	1	0.75	0.286	1

Table 5

Characteristics of heart donors for surviving and non-surviving recipients in the early post-transplant period

Parameters	Heart transplant recipients under 18 years of age		p
	Survivors (n = 79) (mean ± SD)	Deceased (n = 12) (mean ± SD)	
Donor age, years	35.6 ± 11.5	43.6 ± 12.9	0.030
Donor-to-recipient weight ratio	1.40 ± 0.57	1.94 ± 1.45	0.020
Donor-to-recipient height ratio	1.05 ± 0.09	1.21 ± 0.14	<0.0001
Donor-to-recipient BSA ratio	1.24 ± 0.27	1.75 ± 0.46	<0.0001

Abbreviation: BSA, body surface area.

Table 6

Intraoperative characteristics of surviving and non-surviving recipients in the early post-transplant period

Parameters	Heart transplant recipients under 18 years of age		p
	Survivors (n = 79) (Me [Q1; Q3])	Deceased (n = 12) (Me [Q1; Q3])	
Duration of anesthesiological assistance, minutes	390.0 [302.50; 451.00]	565.0 [540.00; 765.00]	<0.0001
Duration of surgical intervention, minutes	290.0 [207.50; 348.75]	475.0 [400.00; 690.00]	<0.0001
Heart transplant ischemia time, minutes	170.5 [135.00; 210.00]	187.50 [162.50; 275.25]	0.007
Duration of CPB, minutes	95.0 [78.75; 120.00]	162.0 [99.0; 189.0]	<0.0001

Abbreviation: CPB, cardiopulmonary bypass.

Deceased recipients demonstrated longer durations of graft ischemia, anesthetic management, surgical intervention, and cardiopulmonary bypass.

DISCUSSION

HT is the standard, definitive therapy for children suffering from various irreversible heart diseases associated with end-stage heart failure. Currently, adult donor transplantation is the only viable option for performing HT in recipients under 18 years of age.

Since January 1, 2012, the Shumakov National Medical Research Center of Transplantology and Artificial Organs has been actively developing a program for pediatric HT from deceased adult donors. The number of pediatric HT has increased from 3 in 2012 to 20 per year in 2024.

Given the high demand for urgent HT, selecting a suitable donor organ within standard criteria is extremely challenging. The global medical community has not developed generally accepted criteria for anthropometric compatibility between an adult donor and a pediatric recipient. Body weight has long been used as a traditional indicator for matching donors to recipients [2]. According to international studies, as the prevalence of childhood obesity increases [3, 4], previous assumptions of a linear correlation between heart size and recipient weight may no longer be accurate. A study by Amdani et al. recommends abandoning donor matching based on recipient weight [5].

The donor-to-recipient height ratio also influences HT outcomes. In the study by Amdani et al., both undersized and oversized donors relative to the recipient were associated with an increased risk of graft dysfunction. However, smaller donor hearts appeared to have a more detrimental impact than larger ones. The authors therefore suggest avoiding donor–recipient height differences exceeding 30% [5].

Matching based on body mass index (BMI) and body surface area (BSA), rather than weight alone, has been associated with improved transplant outcomes [6]. In the present study, the donor-to-recipient BSA ratio was identified as a statistically significant predictor of early post-transplant mortality in recipients under 18 years of age.

Currently, pediatric HT increasingly relies on cross-sectional imaging such as computed tomography (CT) and magnetic resonance imaging (MRI) of both donor and recipient to more accurately assess cardiac chamber dimensions and myocardial thickness. However, in clinical practice, this approach may present significant logistical challenges and can prolong the donor–recipient matching process [5].

A method for donor–recipient matching based on chest X-ray imaging combined with anthropometric parameters (donor weight, height, age, sex) and recipient cardiac dimensions obtained from CT scan has also been reported [7]. Mismatch between donor and recipient anatomical dimensions on cross-sectional CT imaging has been shown to independently influence HT outcomes in pediatric recipients [5].

Additional factors associated with adverse post-transplant outcomes in both adult and children include urgent transplantation status, donor age above 45 years, and intraoperative variables such as prolonged operative time, extended graft ischemia time, and increased intraoperative blood loss [8–11]. These findings are consistent with the results of the present study.

CONCLUSION

In-hospital survival among heart recipients younger than 18 years was 86.8%. The outcomes of HT in children are influenced by the urgency status (UNOS classification) and secondary factors related to it, such as severity of recipient multi-organ dysfunction, donor age, significant anthropometric mismatch between donor and recipient, as well as intraoperative factors including prolonged surgical duration and increased intraoperative blood loss.

The authors declare no conflict of interest.

REFERENCES

1. *Colvin M, Smith JM, Skeans MA et al*. OPTN/SRTR 2014 annual data report: heart. *Am J Transplant*. 2016; 16: 115–140.
2. *Patel A, Bock MJ, Wollstein A, Nguyen K, Malerba S, Lytrivi ID*. Donor-recipient height ratio and outcomes in

pediatric heart transplantation. *Pediatr Transplant*. 2016 Aug; 20 (5): 652–657. doi: 10.1111/petr.12734. Epub 2016 Jun 17. PMID: 27313116.

3. *Cunningham SA, Hardy ST, Jones R, Ng C, Kramer MR, Narayan KMV*. Changes in the Incidence of Childhood Obesity. *Pediatrics*. 2022 Aug 1; 150 (2): e2021053708. doi: 10.1542/peds.2021-053708. PMID: 35789417; PMCID: PMC9879733.
4. *Tsoi MF, Li HL, Feng Q, Cheung CL, Cheung TT, Cheung BMY*. Prevalence of Childhood Obesity in the United States in 1999–2018: A 20-Year Analysis. *Obes Facts*. 2022; 15 (4): 560–569. doi: 10.1159/000524261. Epub 2022 Mar 31. PMID: 35358970; PMCID: PMC9421675.
5. *Amdani S, Aljohani OA, Kirklin JK, Cantor R, Koehl D, Schumacher K et al*. Assessing Donor-Recipient Size Mismatch in Pediatric Heart Transplantation: Lessons Learned From Over 7,500 Transplants. *JACC Heart Fail*. 2024 Feb; 12 (2): 380–391. doi: 10.1016/j.jchf.2023.07.005. Epub 2023 Sep 6. PMID: 37676215.
6. *Conway J, Ballweg JA, Fenton M, Kindel S, Chrisant M, Weintraub RG et al*. Review of the impact of donor characteristics on pediatric heart transplant outcomes. *Pediatr Transplant*. 2020 May; 24 (3): e13680. doi: 10.1111/petr.13680. Epub 2020 Mar 21. Erratum in: *Pediatr Transplant*. 2021 Nov; 25 (7): e14081. doi: 10.1111/petr.14081. PMID: 32198824.
7. *Szugye NA, Zafar F, Ollberding NJ, Villa C, Lorts A, Taylor MD et al*. A novel method of donor–recipient size matching in pediatric heart transplantation: A total cardiac volume–predictive model. *J Heart Lung Transplant*. 2021 Feb; 40 (2): 158–165. doi: 10.1016/j.healun.2020.11.002. Epub 2020 Dec 4. PMID: 33317957; PMCID: PMC7855742.
8. *Foroutan F, Alba AC, Guyatt G, Duero Posada J, Ng Fat Hing N, Arseneau E et al*. Predictors of 1-year mortality in heart transplant recipients: a systematic review and meta-analysis. *Heart*. 2018 Jan; 104 (2): 151–160. doi: 10.1136/heartjnl-2017-311435. Epub 2017 Aug 30. PMID: 28855271.
9. *Westbrook TC, Morales DLS, Khan MS, Bryant R, Castleberry C, Chin C, Zafar F*. Interaction of older donor age and survival after weight-matched pediatric heart transplantation. *J Heart Lung Transplant*. 2017 May; 36 (5): 554–558. doi: 10.1016/j.healun.2016.11.009. Epub 2016 Dec 1. PMID: 28073609.
10. *Hickner B, Anand A, Godfrey EL, Dunson J, Reul RM, Cotton R et al*. Trends in Survival for Pediatric Transplantation. *Pediatrics*. 2022 Feb 1; 149 (2): e2020049632. doi: 10.1542/peds.2020-049632. PMID: 35079811.
11. *Mah D, Singh TP, Thiagarajan RR, Gauvreau K, Piercey GE, Blume ED et al*. Incidence and risk factors for mortality in infants awaiting heart transplantation in the USA. *J Heart Lung Transplant*. 2009 Dec; 28 (12): 1292–1298. doi: 10.1016/j.healun.2009.06.013. Epub 2009 Sep 26. PMID: 19782580; PMCID: PMC4269350.

The article was submitted to the journal on 6.12.2025