Iron Status and Adverse Outcomes in Pediatric Patients After Congenital Cardiac Surgery

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No conflict of interest to disclose

Background-Iron deficiency in children

- **Iron deficiency is the most prevalent micronutrient deficiency in children, with a prevalence of 10% to 30% in children aged 6 months to 5 years.**
- **Associated with developmental delays, behavioral disturbances, impaired immune function.**
- **Increase cardiovascular morbidity and mortality.**

Lancet 2021;397:233-248.
Nutrients 2016;8:330.
Eur J Heart Fail 2017;19:340-347.

Background-Congenital heart disease and Iron status

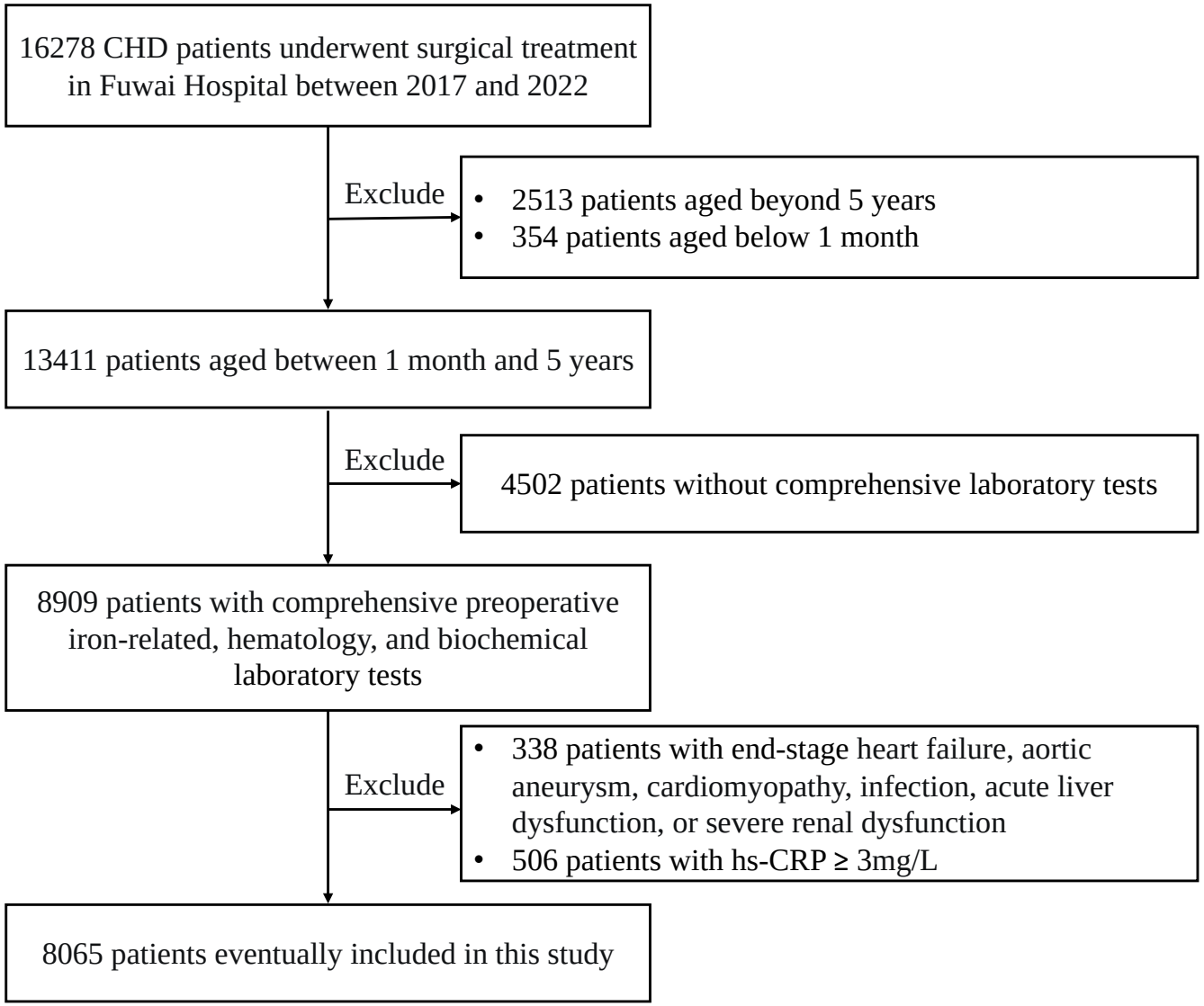
- **Congenital heart disease, the most prevalent birth defects worldwide and leading causes of death among children under 5 years.**
- **Iron status of pregnant women is associated with increased risk of CHD offspring**
- **Association of preoperative iron status and adverse events after congenital cardiac surgery remains unclear**

Int J Epidemiol 2019;48:455-463.
Lancet Child Adolesc Health 2020;4:185-200.
Front Cardiovasc Med 2022;9:887535.

Objective

To Explore the association of preoperative iron status with postoperative outcomes in pediatric CHD patients

Methods-Patients enrollment



Methods-Definition of iron status

- **Iron deficiency**
  - **Ferritin < 15 ng/mL or low transferrin saturation <15% + red cell distribution width (RDW) >16%**
- **Anemia**
  - **Hemoglobin < 110 g/L for children aged 6 months to 5 years (WHO guideline)**
  - **Hemoglobin < 95 g/L for infants aged 1 to 5 months**
- **Iron deficiency anemia**
  - **Meeting both criteria**

Lancet 2021;397:233-248.
Genetics in Medicine 2020;22:317-325.
World Health Organization, 2011
Ann Intensive Care 2017;7:107

Methods-Definition of clinical outcomes

- **Primary outcomes**
  - **In-hospital deaths**

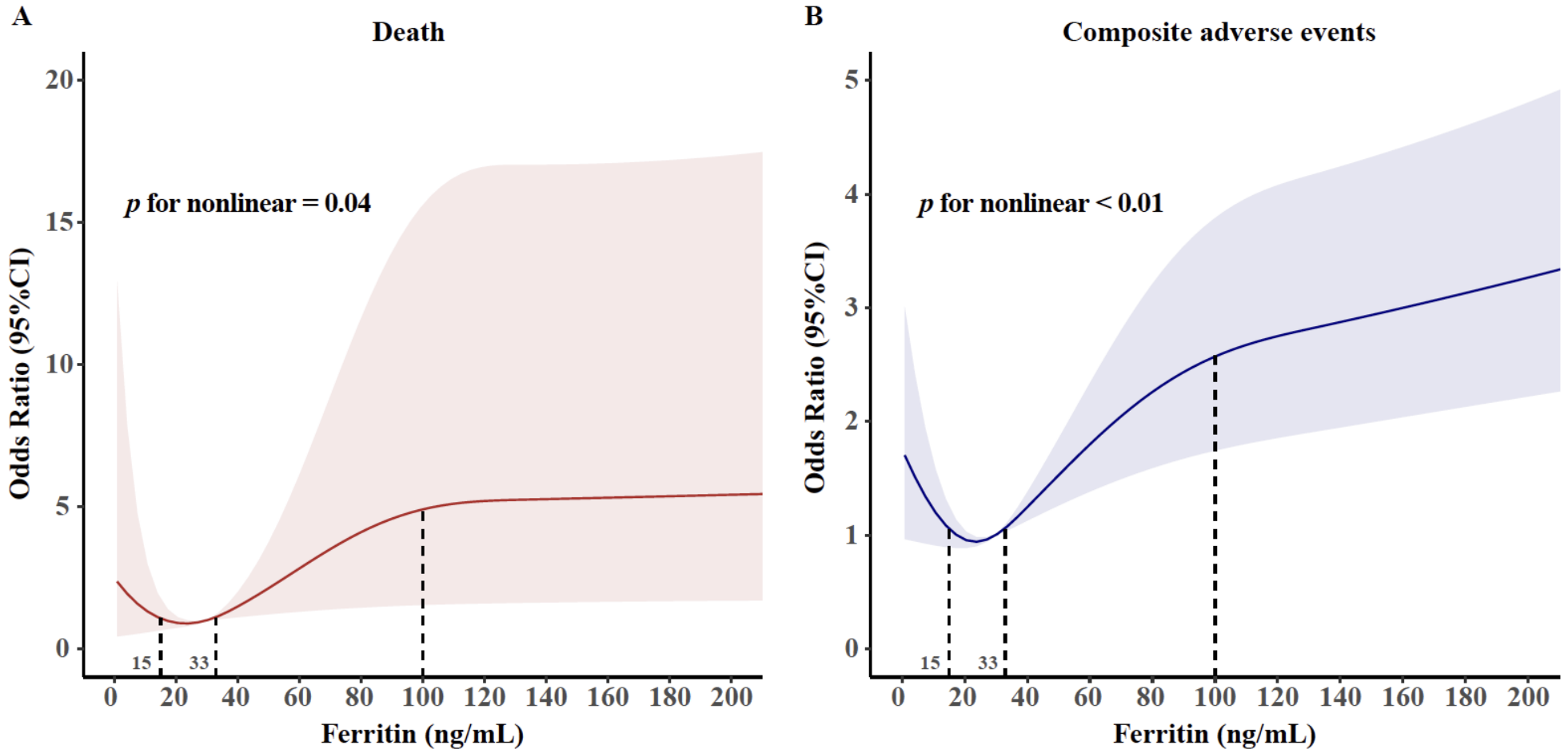
- **Secondary outcomes**
  - **In-hospital deaths**
  - **Abandoned treatment due to critical illness**
  - **Nonscheduled reintervention (pericardial fenestration and exploratory thoracotomy)**
  - **Prolonged mechanical ventilation (more than 2 weeks)**
  - **Prolonged PICU stay (more than 30 days)**
  - **Postoperative ECMO**
  - **Peritoneal dialysis**

Results-Baseline characteristics

	All (n=8065)	Acyanotic CHD (n=6760)	Cyanotic CHD (n=1305)	P-value
Sex, male, n (%)	4003 (49.6)	3233 (47.8)	770 (59.0)	<0.001
BMI (kg/m^2)	15.6 (14.4-16.9)	15.5 (14.4-16.8)	16.1 (14.8-17.6)	<0.001
Age, months	17.3 (7.7-34.7)	19.1 (8.7-35.9)	9.7 (5.9-24.2)	<0.001
1-5 months, n (%)	1354 (16.8)	1011 (15.0)	343 (26.3)	
6 months- 11 months, n (%)	1684 (20.9)	1282 (19.0)	402 (30.8)	
12 months- 23 months, n (%)	1824 (22.6)	1592 (23.6)	232 (17.8)	
24 months- 60 months, n (%)	3203 (39.7)	2875 (42.5)	328 (25.1)	
Iron deficiency, n (%)	1856 (23.0)	1364 (20.2)	492 (37.7)	<0.001
Anemia, n (%)	969 (12.0)	844 (12.5)	125 (9.6)	0.003
Iron deficiency anemia, n (%)	564 (7.0)	465 (6.9)	99 (7.6)	0.359
Ferritin, ng/mL	29.9 (16.9-48.1)	30.4 (18.1-47.9)	26.0 (9.2-49.4)	<0.001
Serum iron, µmol/L	11.3 (8.0-15.3)	11.5 (8.3-15.3)	10.3 (6.0-15.2)	<0.001
Transferrin, g/L	2.7 (2.4-3.0)	2.6 (2.4-2.9)	2.9 (2.6-3.4)	<0.001
Transferrin Saturation, %	19.9 (13.6-27.0)	20.2 (14.3-27.2)	16.9 (8.8-25.6)	<0.001
Hb, g/L	122.0 (113.0-130.0)	121.0 (112.0-128.0)	133.0 (118.0-152.0)	<0.001
RDW, %	13.1 (12.5-14.2)	13.0 (12.4-13.9)	14.1 (12.9-16.8)	<0.001

Results

Association between Ferritin level and clinical outcomes



Restricted cubic spline, right skewed U-shaped

Results

	Iron repletion	Iron deficiency	Intermediate ferritin	High ferritin
Patients, n (%)	2686 (33.3)	1856 (23.0)	2924 (36.3)	599 (7.4)
Death, n (%)	2 (0.1)	10 (0.5)	8 (0.3)	9 (1.5)
OR (95%CI), death	1, reference	3.68 (0.77-17.59)	3.09 (0.65-14.69)	8.20 (1.61-41.86)
P-value, death		0.102	0.156	0.011
Composite events, n (%)	39 (1.5)	74 (4.0)	78 (2.7)	59 (9.8)
OR (95%CI), composite	1, reference	1.80 (1.18-2.73)	1.64 (1.11-2.44)	4.21 (2.65-6.68)
P-value, composite		0.006	0.014	< 0.001

Discussion-Summary

- **Iron status is not only pivotal for the growth and development of children, but also plays a critical role in the prognosis of pediatric patients.**

- **Our findings demonstrated a significant association between preoperative iron imbalance and increased risks of postoperative mortality and composite adverse events**

- **This study represented the largest cohort reporting on the prevalence of iron deficiency and anemia in pediatric patients with CHD.**

Discussion-Largest cohort

- **We identified iron deficiency, anemia, and iron deficiency anemia in 23.0%, 12.0%, and 7.0% of pediatric patients with CHD**

- **Exceed the prevalence reported in United States utilizing data from the 2007–2010 National Health and Nutrition Examination Survey for iron deficiency (7.1%), anemia (3.2%), and iron deficiency anemia (1.1%) among children aged 1–5 years.**

- **Statistical Monitoring Report of the Program for the Development of Chinese Children (2011-2020) released by the National Bureau of Statistics, the prevalence of anemia in children under 5 years old was 5.38%, indicating a relatively high burden of anemia (12.0%) among pediatric CHD patients in China.**

- **Indicating more attention should be paid on the iron status of patients with CHD**

Nutrients 2016;8:330.

National Bureau of Statistics of China. Statistical monitoring report of the Program for the Development of Chinese Children

Discussion-Risk factor

- **An initial evidence highlighting the impact of preoperative iron imbalance on postoperative adverse events in pediatric CHD patients.**

- **Pediatric patients with high iron status increases risks of delayed sexual maturation, retarded growth, progressive liver and heart disease, and a reduced life expectancy, which is also the risk factor for adverse events in pediatric patients with CHD**

- **Preoperative ferritin of approximately 25 ng/mL was indicative of the minimal risk for postoperative complications, which suggest the potential preoperative iron supplementation.**

Clin Exp Pediatr 2023;66:98-109.

Take home message

- **Iron deficiency, anemia, and iron deficiency anemia were observed in 23.0%, 12.0%, and 7.0% of patients, respectively.**
- **Iron imbalance is associated with adverse outcomes in pediatric CHD patients**
- **It is worthwhile to investigate the potential benefits of administering iron supplements before pediatric cardiac surgery.**

Thank you!