

Enhanced Discrimination of Myocardial Injury in a Pediatric Population Using Age-Specific Biomarker Reference Intervals

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Pediatric heart disease encompasses a spectrum of heart conditions presenting in children, including myocarditis and congenital heart defects or abnormalities. In addition to echocardiography and electrocardiograms, biomarkers of myocardial injury are used to help in diagnosis. Following diagnosis, treatment plans can involve medications, surgical procedures, and in serious cases, even heart transplant.

The most common biomarker used in evaluation of pediatric heart disease is high-sensitivity cardiac troponin I (hs-cTnI). However, in the absence of age-specific reference intervals for pediatric patients, clinicians often diagnose these patients using the adult reference interval for hs-cTnI. This practice can result in misdiagnosis and prompt the need for further investigation, including multiple blood draws on very young patients and outpatient visits, which can be distressing for patients and their families, while also very costly.

Understanding that age-specific reference intervals for hs-cTnI could increase the accuracy of myocardial injury clinical diagnosis in pediatric patients, a multidisciplinary clinical care team from Shandong Yantai Yuhuangding Hospital in China undertook a collaborative effort to establish and implement age-specific reference intervals for pediatric patients. The pediatric medicine, pediatric surgery, neonatology and IT departments collaborated to establish and implement the new reference intervals into clinical decision-making.

Historically, the direct determination of reference ranges in pediatric populations has been impeded due to insufficient numbers of healthy children participating in studies. Therefore, the multidisciplinary care team mined laboratory data using the indirect Hoffman method to establish a reference interval for hs-cTnI in children. The team established reference ranges of hs-cTnI corresponding to specific ages, which were provided directly to clinical departments through the laboratory information system.

Integration of the new reference interval into routine evaluations in this initiative permitted the safe rule out myocardial injury in a vulnerable pediatric population, with the safe exclusion of myocardial injury increasing from 52.62% to 82.88% in patients from birth to 2 days of age; from 55.46% to 96% in patients 2 to 7 days old; and from 59.96% to 82.59% for patients between 7 days



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and 2 months of age. Thus, many children who would have previously been misdiagnosed as having myocardial injury are now identified as having an hs-cTnI in the normal range.

“The new reference interval for pediatrics allows me to safely rule out cardiac problems in children, reducing the pain of multiple blood draws in children and alleviating the anxiety of parents,” said Dr. Yanjie Ding, Director of Neonatology and Vice Director of Pediatrics.

The development and application of age-specific references improved clinician sentiment across neonatology, pediatrics, pediatric surgery, cardiac surgery and cardiovascular medicine, with 93.3% of survey respondents stating the use of the new pediatric reference interval improved their confidence in clinical decision-making.

Additionally, the ability to rule out myocardial injury in pediatric patients decreased the need for additional testing such as echocardiograms, electrocardiograms and further biomarker testing, leading Shandong Yantai Yuhuangding Hospital to realize an 84% reduction in myocardial biomarker blood tests in the neonatology and pediatrics departments.

The early rule-out of myocardial injury also removed the unnecessary cost of prophylactic nutritional myocardial drug therapies, saving an estimated \$248.35 per patient with myocardial injury safely ruled out.

“We are the first hospital in China that used laboratory Big Data to establish reference interval of hs-cTnI for children,” said Dr. Chenming Sun, Director of the Laboratory Center and Chief Laboratory Technician. “We shared the practice in many important national academic forums on multidisciplinary cooperation in laboratory and clinical practice. Inspired by this, several other hospitals in China have also initiated the practice.”

Increased use of this best practice at more hospitals would allow the aggregation of national multicenter data, greatly increasing the reliability of the hs-cTnI reference interval in children and enabling more children to benefit from it.

By innovatively tapping into laboratory data to establish a more reliable basis for clinical diagnosis of myocardial injury in children, the initiative contributed to advancing patient care and earned recognition of achievement from the 2021 UNIVANTS of Healthcare Excellence award program.

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