Perioperative NT-proBNP level: Potential prognostic markers in children undergoing congenital heart disease surgery

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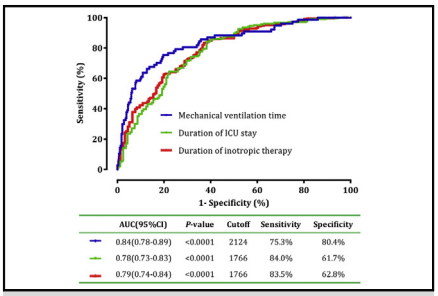
ABSTRACT

Objectives: To assess the relationship between N-terminal pro–brain natriuretic peptide (NT-proBNP) levels at different time points and early outcome, and to evaluate the reliability of NT-proBNP level as a predictor of early outcome after surgery in a large series of children with congenital heart disease (CHD).

Methods: A retrospective observational study involving 363 consecutive children with CHD was used. Plasma NT-proBNP records were obtained for each patient before and 1, 12, and 36 hours after surgery. The specificity, sensitivity, and prediction value of NT-proBNP in predicting early postoperative outcomes were determined.

Results: Analyses confirmed that time-varying NT-proBNP level, particularly 1-hour postoperative levels, had prognostic value on the prediction of prolonged duration of mechanical ventilation, intensive care unit (ICU) stay, and inotropic therapy. Joint modeling analyses of a linear mixed effects model for NT-proBNP from before to 36 hours after surgery and generalized linear models for the duration of the mechanical ventilation, ICU stay, and inotropic therapy showed that a 1% increase in NT-proBNP was associated with 5.5%, 3.9%, and 3.5% relative increases in expected duration of mechanical ventilation, ICU stay, and inotropic therapy, respectively; related *P* values were .001, .001, and .01, respectively.

Conclusions: After CHD surgery, the perioperative NT-proBNP levels might be powerful markers to identify subjects at higher risk for worse outcome. (J Thorac Cardiovasc Surg 2017;154:631-40)



ROC curve for 1-hour NT-proBNP predicting ventilation >48 hours, ICU stay, and inotropic therapy >3 days.

Central Message

For children after CHD surgery, perioperative NT-proBNP levels might be early, accurate, and sensitive predictors of prolonged ventilation, ICU stay, and inotropic support duration.

Perspective

We found that perioperative NT-proBNP levels, particularly 1-hour postoperative levels, were correlated with duration of mechanical ventilation, ICU stay, and inotropic therapy. We used joint models to quantify the degree of the correlation between perioperative NT-proBNP level and the length of mechanical ventilation, ICU stay, and inotropic therapy. It will help clinicians to predict early outcome and plan their therapeutic protocols more quickly after surgery.

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Although great progress has been made, surgical intervention for the treatment of children with congenital heart disease (CHD) is still carrying significant early and late

Scanning this QR code will take you to a supplemental video for the article.

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Abbreviations and Acronyms

ACC = aorta crossclamp
AKI = acute kidney injury
AUC = area under the curve
CHD = congenital heart disease
CICU = cardiac intensive care unit
CPB = cardiopulmonary bypass
DHCA = deep hypothermic circulatory arrest
ICU = intensive care unit
LCOS = low cardiac output syndrome
LME = linear mixed effects
LRS = left to right shunt
MCMC = Markov chain Monte Carlo
NT-proBNP = N-terminal pro–brain natriuretic peptide
PAH = pulmonary artery hypertension
RACHS-1 = the Risk Adjustment in Congenital Heart Surgery, version 1
ROC = receiver operating characteristic
STAT = Society of Thoracic Surgery-European Association for Cardio-Thoracic Surgery
TGA = d-transposition of the great arteries
TOF = tetralogy of Fallot
UVH = univentricular heart
VSD = ventricular septal defect

morbidity and mortality. Making the continued search for improved prognostic biomarkers besides commonly measured clinical and physiologic parameters is of increasing importance of children admitted to intensive care units (ICUs) after surgery for CHD. Accumulating evidence suggests that both active B-type natriuretic peptide (BNP) and inactive N-terminal pro-BNP (NT-proBNP) have been shown to have prognostic value in adults with cardiac diseases (eg, chronic congestive heart failure and acute myocardial infarction), and to predict morbidity and major adverse cardiac events after adult heart surgery.

Recently, more concerted efforts for the prognostic value of BNP/NT-proBNP after surgical intervention for CHD in pediatrics have also occurred.[1] For example, Hsu and coauthors[2] found that BNP level of 1 or greater at 24 hours after cardiac surgery in neonates was correlated with poor postoperative outcome, including low cardiac output syndrome, fewer ventilator-free days, and 6-month major adverse cardiac events. Niedner et al[3] reported that higher levels of early postoperative BNP were associated with longer inotropic requirement and hospitalization in children after surgery for single-ventricle CHD. Nahum and colleagues[4] reported similar results in a prospective comparative study on 19 infants aged 1 to 12 months with CHD undergoing complete repair. In a prospective study on 587 children undergoing cardiac surgery, Cantinotti et al[5] showed independent and incremental prognostic value of BNP in pediatric cardiac surgery, supporting its routine use in this setting.

However, current evidence is limited to BNP.[6] Despite the equivalence in clinical efficacy of BNP and NT-proBNP supported by many studies, significant differences between circulatory levels has been reported for any given disease state.[7,8] To our knowledge, besides a few studies focusing on the role of NT-proBNP in pediatric patients with cardiac disease,[9] there are much fewer data on the prognostic value of perioperative NT-proBNP levels in children after surgical repair of structural congenital heart defects, particularly large-scale studies with high statistical power.

Therefore, the primary objectives of this article were to determine and (1) to investigate potential patterns of association between perioperative circulating NT-proBNP levels and early outcomes after repair of congenital heart defects and (2) to evaluate the reliability of NT-proBNP level as a predictor for postoperative outcomes in a large series of children undergoing cardiac surgery for CHD.

PATIENTS AND METHODS

Subjects

The clinical information system databases of the Guangzhou Women and Children's Medical Center were scanned for pediatric patients enrolled for cardiac surgery having CHD. Patients younger than 18 years with CHD who underwent cardiac surgery were eligible for the study. Children who had preoperative arrhythmia (potentially malignant ventricular arrhythmias and high-degree atrioventricular block), rheumatic heart disease, infective endocarditis, myocarditis, pericardial disease, renal dysfunction, or neoplasms,[10-12] or who could not be separated from cardiopulmonary bypass (CPB) were excluded.

Between June and December 2014, 415 eligible consecutive patients undergoing corrective or palliative CHD surgery at the Department of Pediatric Cardiac Surgery and admitted to the Cardiac Intensive Care Unit (CICU) at the Guangzhou Women and Children's Medical Center, Guangzhou, were identified. However, to display the results in a more homogeneous population, we excluded 38 cases without CPB and 14 single-ventricular cases from the final analysis according to the reviewers. Thus, results from 363 cases were presented in the current study. The institutional review board at the Guangzhou Women and Children's Medical Center reviewed and approved this study.

Clinical Procedure

The preoperative anesthesia management, surgical procedure (including sternotomy, establishing CPB, correction of cardiac defects, closure of thoracic cavity, and suturing the skin; Video 1), and subsequent CICU management followed standard institutional practices. All patients were admitted to the CICU intubated and mechanically ventilated after operation. If postoperative urine output was less than 0.5 mL/kg per hour lasting for more than 2 to approximately 4 hours under the premise of the application of diuretics, peritoneal dialysis was adopted until the urine output was more than 2 mL/kg per hour, blood urea nitrogen, creatinine, and electrolytes were maintained in the normal range. Termination of the surgical procedure means ending with suturing the skin.

Sample and Data Collection

Blood samples were obtained from an arterial catheter preoperatively and at 1, 12, and 36 hours after the surgical procedure at CICU according