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POTENTIAL USEFULNESS OF N-TERMINAL PRO- BRAIN NATRIURETIC PEPTIDE LEVEL IN CONGENITAL HEART SURGERY

To the Editor:

In a recent article, Qu and colleagues¹ reported their observations on the relationship between N-terminal pro-brain natriuretic peptide (NT-proBNP) levels at different time points and early outcome in an attempt to evaluate the reliability of NT-proBNP level as a predictor of early outcome after congenital heart surgery. It would certainly be useful to have such a tool available in the perioperative management of children with congenital heart defects undergoing surgery, but there is probably space for improvement in the proposed methodology.

Qu and colleagues¹ failed to define some of the exclusion criteria, such as renal dysfunction, for which no laboratory results or cutoff points were specified. This point is quite important, considering the relatively high incidence of renal dysfunction in children with congenital heart defects.² Because NT-proBNP is produced by other cells in the body for various reasons (renal dysfunction being among them), confounding factors in its measurement should be avoided whenever possible.

Other undefined information included details of inotropic support, which was limited to the duration but without data on the vasoactive inotropic score, which would give more accurate information about the relationships between patient's condition and the corresponding NT-proBNP levels.

No objective assessment of the ventricular function was provided, only the Risk Adjustment in Congenital Heart Surgery 1 score, with 75% of children scored as I or II, 25% as III or IV, and none as V or VI. Not only was the more precise Aristotle Comprehensive Complexity score not used, even if this point had been included in the limits of the study, all patients at high risk were still excluded.³

The Editor welcomes submissions for possible publication in the Letters to the Editor section that consist of commentary on an article published in the Journal or other relevant issues. Authors should: • Include no more than 500 words of text, three authors, and five references. • Type with double-spacing. • See <http://jtcvs.ctsnetjournals.org/misc/fora.shtml> for detailed submission instructions. • Submit the letter electronically via jtcvs.editorialmanager.com. Letters commenting on an article published in the JTCVS will be considered if they are received within 6 weeks of the time the article was published. Authors of the article being commented on will be given an opportunity to offer a timely response (2 weeks) to the letter. Authors of letters will be notified that the letter has been received. Unpublished letters cannot be returned.

The results were expressed as percentages, without indicating the full numbers that would probably have better illustrated the interpatient variability in NT-proBNP levels and whether they were relevant.

Finally, Qu and colleagues¹ concluded that NT-proBNP value could be correlated with prognostic information on expected outcomes, even though further studies will be required establish the statistical significance. How can this conclusion provide inferences for the application of this value in daily clinical practice? Ultimately, knowing the NT-proBNP levels could have a potential utility only if it could be used to modify the treatment of the patients, which was not demonstrated by Qu and colleagues.¹

In summary, it was extremely important to present this specific biomarker as a potential tool in the post-operative management of congenital cardiac patients. To validate the clinically utility of NT-proBNP level, however, further investigations into its prognostic ability are required in a larger, more heterogeneous patient population.

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THE PROGNOSTIC ROLE OF NATRIURETIC PEPTIDES IN CHILDREN UNDERGOING CARDIAC SURGERY:

CAN ACUTE KIDNEY INJURY AFFECT THEIR ACCURACY?

Reply to the Editor:

Recent evidence supports the use of brain natriuretic peptide (BNP) and N-terminal pro-BNP as prognostic

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markers in children undergoing cardiac surgery for congenital heart defects.¹⁻⁴ Acute kidney injury (AKI) is a common and serious complication after cardiac surgery^{1,5} that may greatly affect costs, morbidity, and mortality. The AKI complicating cardiac surgery is considered to be a consequence of complex interactions between cardiac and renal injury, also known as *cardiorenal syndromes*.⁶⁻⁸ Renal damage after cardiac surgery is a consequence of multiple factors, including renal ischemia-reperfusion damage, systemic inflammatory response caused by cardiopulmonary bypass, hemodynamic instability after surgery, and use of potentially nephrotoxic drugs (such as loop diuretics).⁶⁻⁸ Not only does hemodynamic unbalance compromise kidney function, renal dysfunction has negative consequences on cardiac function⁶⁻⁸ through complex neurohormonal feedback mechanisms. Cardiac surgery thus may provoke a vicious circle in which heart and kidney dysfunction initiate, perpetuate, and aggravate each other.⁶⁻⁸

In this situation, it may be difficult to understand how much of the postoperative increase in BNP values is due to heart failure itself and how much to renal damage.⁹ The causes of BNP increases in patients with renal failure are not known. A study in 1994 on 103 adult patients with chronic, non-dialysis-dependent renal failure and 60 adult control patients with hypertension but without renal failure indicated that elevated BNP in patients with renal failure primarily reflect underlying left ventricular dysfunction, rather than severity of renal dysfunction.⁹

In 135 children undergoing cardiac surgery (median age, 7 months; interquartile range, 1-49 months), the frequency of AKI was 39%.¹ In particular, AKI occurred in 65% of neonates versus 32% of older children ($P = .004$). Children with AKI also showed significantly higher ($P = .001$) values of BNP than did patients without AKI.¹ Furthermore, BNP values at 12 hours after surgery were also significantly correlated with 2-hour urinary neutrophil gelatinase-associated lipocalin ($p = 0.321$; $P < .001$), an early marker of kidney injury. These data suggest a close link between cardiovascular and renal damage. BNP increase after surgery was more closely associated with the severity of congenital heart defects, however, especially in neonates requiring urgent surgery, than with renal damage.¹ Quali and colleagues,¹⁰ in a study that included only 35 children undergoing hemodialysis for renal disease, reported that BNP was correlated with ejection fraction and remained an independent prognostic marker of adverse outcome.

Of interest, BNP has been proved to be an independent prognostic marker of major complications^{1,3,4} and of prolonged mechanical ventilation and intensive care stay¹⁻⁴ in children undergoing cardiac surgery.¹⁻⁴ Studies evaluating correlations of BNP with kidney injury in pediatric cardiac surgery,^{1,11} however, failed to prove the prognostic value of natriuretic peptides for the development of AKI in the postoperative setting.^{1,11}

In summary, AKI certainly influences the BNP-NT-pro-BNP response after pediatric cardiac surgery. The rise and the trend of natriuretic peptide values, however, seems to be independent of the renal damage.¹

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