Does heart-type fatty acid-binding protein predict clinical outcomes after pediatric cardiac surgery?

Egmond S Evers, Varsha Walavalkar[1], Suresh Pujar[1], Latha Balasubramanian[1], Frits W Prinzen, Tammo Delhaas, Ward Y Vanagt, Shreesha Maiya[1]

Departments of Physiology and Biomedical Engineering, Cardiovascular Research Institute Maastricht, Maastricht University, Maastricht, The Netherlands, [1]Department of Pedicatric Cardiology, Narayana Institute of Cardiac Sciences, Bengaluru, Karnataka, India

ABSTRACT

Introduction : **The early identification of vulnerable pediatric cardiac surgery patients can help clinicians provide them with timely support. Heart-type fatty acid-binding protein (H-FABP) is an early biomarker of myocardial injury in acute myocardial infarction in adults. In this study, we evaluated the correlations between postoperative H-FABP, creatine kinase-myocardial band (CK-MB), troponin-I, total bypass time, and clinical outcomes.**

Methods : **In 32 pediatric patients that underwent ventricular septal defect closure we measured H-FABP, troponin-I and CK-MB preoperatively and 1, 3, and 6 h after aortic declamping. Spearman's Rho correlations were calculated between laboratory and clinical parameters including inotropic support duration, aortic cross-clamp time, total bypass time, ventilation-weaning-time, and total Intensive Care Unit stay.**

Results : **H-FABP, CK-MB, troponin-I, and total bypass time have a similarly weak to moderate correlation with clinical outcome measures.**

Conclusions : **The predictive value of H-FABP for clinical outcome is not stronger than that of CK-MB, Troponin-I, or bypass times.**

Keywords : Bypass time, heart-type fatty acid-binding protein, pediatric cardiac surgery

INTRODUCTION

In spite of advances in cardiopulmonary bypass with various cardioprotective techniques, significant morbidity and mortality remain following open heart surgery in children.[1] Heart-type fatty acid-binding protein (H-FABP) is a small cytoplasmic protein (15 kDa) released from cardiac myocytes following myocardial injury.[2,3] H-FABP is a very early marker of myocardial injury, reaching its peak release within 1 h in adult myocardial infarct patients. We evaluated the potential of H-FABP as a predictor of clinical outcome in children undergoing cardiac surgery, as compared with the more slowly released cardiac injury markers (creatine kinase-myocardial band [CK-MB] and troponin-I, both peaking 3–6 h after injury) and as compared with total bypass time.

METHODS

This is a retrospective study of laboratory and patient file data from a blinded randomized, controlled trial (RCT) that was performed at Narayana Institute of Cardiac Sciences, Bengaluru, India, in accordance with the Helsinki Declaration. It was

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Address for correspondence: Dr. Ward Y Vanagt, Cardiovascular Research Institute Maastricht, Universiteitssingel 50, 6229ER Maastricht, The Netherlands. E-mail: ward.vanagt@maastrichtuniversity.nl

approved by the Institutional Ethical Committees and registered (CTRI/2014/03/004468).[4]

Children 1–16 years undergoing surgical ventricular septal defect closure were included in an RCT with sildenafil preconditioning aiming to reduce ischemia/reperfusion injury.[4] As no significant differences between sildenafil and placebo were found, all patients were pooled together for the current analysis. Serum CK-MB, troponin-I, and H-FABP were measured at baseline and at 1, 3, and 6 h after aortic declamping. CK-MB and troponin-I were assessed by chemiluminescence immunoassay (Siemens Healthcare Diagnostics, East Walpole, USA). H-FABP samples were centrifuged and stored at −20°C, to be measured in an external laboratory after the study using immunoturbidimetry (Randox Laboratories Limited, County Antrim, United Kingdom). Per- and post-operative measurements of aortic cross-clamp (ACC) time, bypass time, ventilation-weaning time, inotropy time, and Intensive Care Unit (ICU) stay were noted. Echocardiographic left ventricular ejection fraction (LVEF) was assessed 5–7 days after surgery, before discharge. The area under the curve (AUC) was calculated for the injury marker release using a trapezoidal method.[4] We calculated Spearman's rank correlations (rho) because of small sample size, nonnormal data distribution, and unknown relationship nature between the parameters. We considered correlation coefficients as follows: 0–0.19: Very weak, 0.2–0.39: Weak, 0.4–0.59: Moderate, 0.6–0.79: strong, and 0.8–1: Very strong.

RESULTS

Of 39 patients participating in the RCT,[4] seven were excluded for missing sample (s). The remaining patients' data were expressed as median (interquartile range Q1–Q3). The median age at surgery was 47 months (24–94), ACC time 30 min (26–36), bypass time 57 min (50–67), ventilation-weaning time 116 min (87–362), inotropy time 26 h (20–38), ICU stay 38 h (25–47), and predischarge LVEF 64% (60–66). There was no mortality or other major adverse outcome in any of the patients.

All three cardiac biomarkers had poor to moderate correlations with clinical outcome parameters, including ICU-stay, inotropy time, and LVEF. Bypass time, which is often considered a predictor of postoperative morbidity and mortality in clinical practice, showed an equally poor to moderate correlation with biomarkers and clinical parameters.

There was a strong correlation between the three injury markers. For all three injury markers, there was a very strong correlation between the peak value and the respective AUC (correlation coefficients between peak and AUC for CK-MB 0.99, troponin-I 0.99, H-FABP 0.97). Table 1 and Figure 1 contain detailed results.

DISCUSSION

Postoperative cardiac biomarker release can be attributed to ischemia and reperfusion injury, but also to manipulation and direct myocardial injury during surgery. In accordance with previous reports,[2] H-FABP showed an early rise and peak after the time of injury, i.e., following ACC release. Despite its different release pattern, H-FABP had a strong correlation with the other cardiac biomarkers CK-MB and troponin-I, which peaked at 3 h after ACC release in almost all patients.

The observed negative correlation between age and cardiac biomarker release may be due to the higher sensitivity of younger myocardium to ischemia-reperfusion injury,[5] or

Table 1: Spearman's rank correlation coefficients (rho)

Parameter	Statistic parameter	Age	ACC time	Bypass time	Ventilation weaning time	ICU stay	Inotropy time	CK-MB AUC	Troponin-I AUC	H-FABP AUC
Age	CC	1.00	−0.15	−0.33	0.09	−0.04	−0.30	−0.33	−0.48	−0.58
	Sign*		0.41	0.06	0.61	0.83	0.09	0.06	0.005	0.001
ACC time	CC	−0.15	1.00	0.75	0.10	0.07	0.36	0.47	0.49	0.44
	Sign*	0.41		0.00	0.58	0.68	0.040	0.006	0.005	0.012
Bypass time	CC	−0.33	0.75	1.00	0.19	0.17	0.54	0.46	0.46	0.51
	Sign*	0.06	0.000		0.31	0.35	0.002	0.008	0.008	0.003
Ventilation	CC	0.09	0.10	0.19	1.00	0.45	0.54	−0.08	0.06	0.07
weaning time	Sign*	0.61	0.58	0.31		0.010	0.002	0.67	0.73	0.70
ICU stay	CC	−0.04	0.07	0.17	0.45	1.00	0.69	0.22	0.21	0.16
	Sign*	0.83	0.68	0.35	0.010		0.000	0.24	0.25	0.37
Inotropy time	CC	−0.30	0.36	0.54	0.54	0.69	1.00	0.32	0.45	0.37
	Sign*	0.09	0.040	0.002	0.002	0.000		0.08	0.010	0.040
CK-MB AUC	CC	−0.33	0.47	0.46	−0.08	0.22	0.32	1.00	0.72	0.80
	Sign*	0.06	0.006	0.008	0.67	0.24	0.08		0.000	0.000
Troponin-I AUC	CC	−0.48	0.49	0.46	0.06	0.21	0.45	0.72	1.00	0.77
	Sign*	0.005	0.005	0.008	0.73	0.25	0.010	0.000		0.000
H-FABP AUC	CC	−0.58	0.44	0.51	0.07	0.16	0.37	0.80	0.77	1.00
	Sign*	0.001	0.012	0.003	0.70	0.37	0.040	0.000	0.000	

*Sign: *P* value. CCs between the injury markers are depicted in darker colors when the CC was>0.40 (i.e., moderate, strong or very strong correlation). The table contains original data only. CK-MB: Creatine kinase myocardial band, H-FABP: Heart-type fatty acid-binding protein, ACC: Aortic cross clamp, ICU: Intensive Care Unit, AUC: Area under the curve, CCs: Correlation coefficients

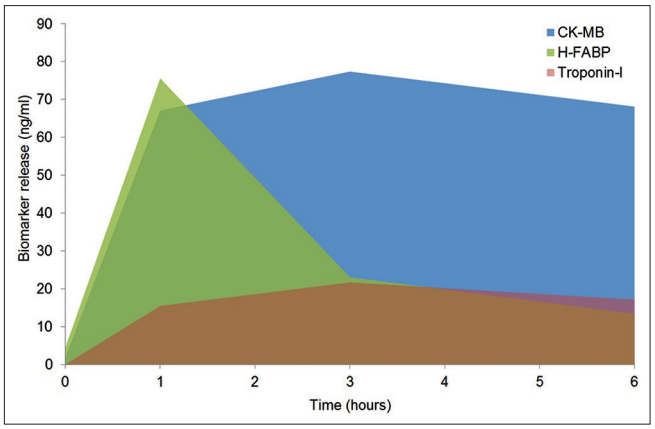

Figure 1: Median cardiac biomarker release after pediatric heart surgery

due to the fact that operations on small hearts may require somewhat longer bypass times and more manipulation.

One previous pediatric study by Hasegawa *et al.* has compared the injury markers H-FABP, CK-MB, and troponin-T and their correlation with postoperative outcome.[6] The Hasegawa *et al.* article found similar good correlations between the injury markers but differed with our study by finding a correlation between H-FABP release and postoperative outcome (especially increased inotropic needs).[6] This is probably accounted for by the fact that the Hasegawa *et al.* study[6] included more complex operations (including double outlet right ventricle, Tetralogy of Fallot, valvular disease, and atrioventricular septum defects) and had considerably longer cross-clamp times (mean 77 min) and cardiopulmonary bypass times (mean 146 min) than our study. Furthermore, the larger number of studied patients by Hasegawa (n = 100) may have enabled them to detect differences that were not revealed in our smaller study.

Limitations

The small sample size and short bypass times in relatively simple cardiac surgery demand caution in extrapolating conclusions to complex, longer operations. Given the limitations of this study, research including a larger sample of longer, more complex operations may serve to more definitively provide guidance on the usefulness of H-FABP in care for pediatric patients after cardiac surgery.

CONCLUSION

H-FABP was not proven to be a clinically useful predictor of clinical outcomes in pediatric cardiac surgery in this study. H-FABP shows similarly poor-moderate correlations with clinical outcomes compared with CK-MB, troponin-I, and cardiopulmonary bypass time. Therefore, we consider that it is not justified to perform repeated, invasive, and costly additional testing in clinical practice.

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Conflicts of interest

There are no conflicts of interest.

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