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Relationship Between Natriuretic Peptides and Hemodynamic Parameters Following Heart Surgery in Infancy

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1. Introduction

Critically ill states, perioperative period of major surgery, particularly cardiac operations are often encountered with large hemodynamic alterations and fluid shifts. Cardiac failure in patients with congenital heart defect has heterogeneous origin therefore diagnosis related treatment is difficult to apply. During the postoperative period, hemodynamic instability has multifactorial origin and cardiorespiratory dysfunction has several manifestation e.g. myocardial dysfunction, pulmonary hypertension etc (Laussen & Roth, 2003).
Biochemical markers play an important role in the risk stratification of patients with cardiovascular disease. Elevated brain natriuretic peptide level has been shown to reveal congestive heart failure among adult patients admitted to emergency department with dyspnoe (Maisel et al, 2002; de Lemos et al, 2001), and to predict adverse events in acute coronary syndromes (de Lemos et al, 2001). Cardiac troponin, creatine kinase-MB, brain natriuretic peptide and C-reactive protein have been shown to predict mortality and morbidity in unstable coronary artery disease (Lindahl et al, 2000). In patients with pulmonary embolism, brain natriuretic peptide and other cardiac markers, such as troponin predict adverse outcomes much more accurately than any other clinical signs (Kucher et al, 2003). In the last decade, several papers investigating the prognostic, diagnostic and therapeutic relevance of natriuretic peptides in the pediatric population have been published (in rev. Cantinotti et al, 2011; Cantinotti et al, 2011).

2. Physiology of the natriuretic peptides

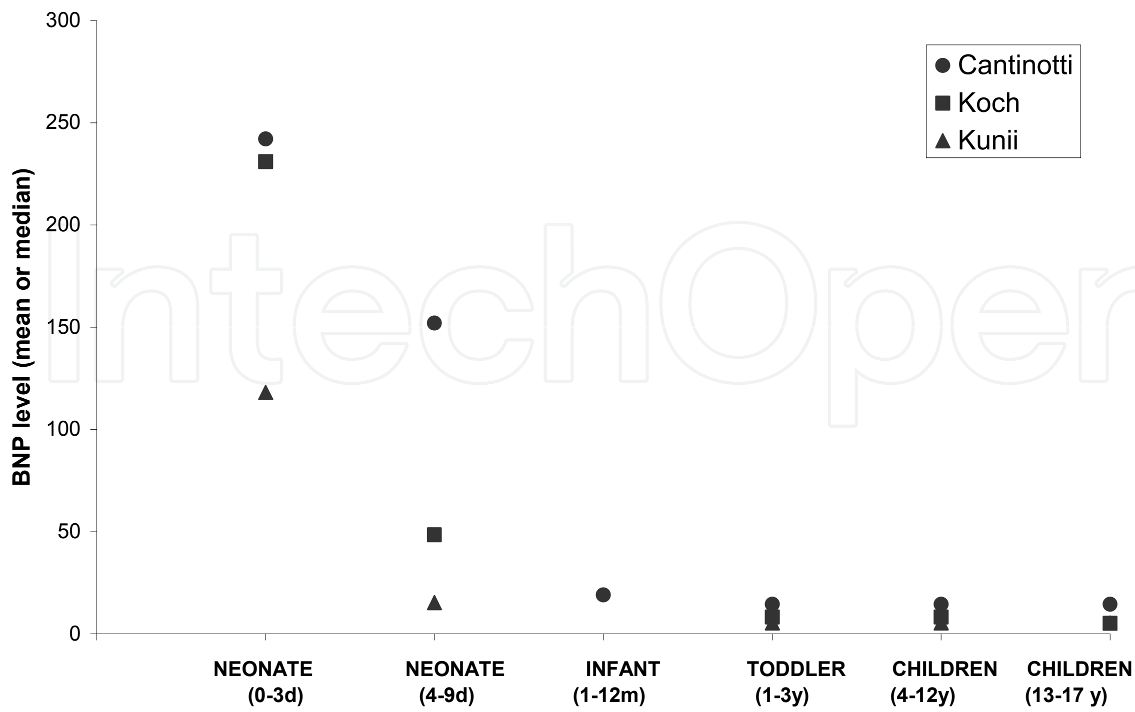
The natriuretic peptides are a family of peptides produced by the myocardium, vascular endothelium and the kidneys (Clerico et al, 2006). The “hormone” of the heart is involved in the regulation of intravascular homeostasis, myocardial function. On the other hand, natriuretic peptides counteract with the renin-angiotensin-aldosterone system, symphathetic nervous system, vasopressin release. Receptors of natriuretic peptides are mainly presented in the myocardium, kidneys, lungs and vascular endothelium. The action is mediated by c-

GMP, the cytoplasmatic calcium availability will be decreased in the smooth muscles and it will result in vasodilatation.(Silberbach & Roberts, 2001).
Atrial stretching triggers release of the preformed prohormone of atrial natriuretic peptide (NT-proANP) in the atrial wall. During secretion, the prohormone of atrial natriuretic peptide (ANP) is cleaved to atrial natriuretic peptide and N-terminal pro-atrial natriuretic peptide (Kangawa et al, 1984). Although brain natriuretic peptide chemically resembles atrial natriuretic peptide to some extent, it is synthetized both in the atrial and ventricular myocardium due to volume and pressure overload. The production of BNP requires time (6-12 hours), since RNA transcription of the prohormone precedes the secretion. Then, the prohormone of brain natriuretic peptide is cleaved to brain natriuretic peptide (BNP) and N-terminal pro-brain natriuretic peptide (NT-proBNP). N-terminal peptides have several times higher concentrations and longer half life time in blood circulation than atrial natriuretic peptide and brain natriuretic peptide, making them reliable markers (Ham et al, 1995).

3. Diagnostic application of the natriuretic peptides

3.1 Adult population

In adults, diastolic dysfunction or asymptomatic aortic stenosis confirmed by echocardiography or angiography show marked correlations with brain natriuretic peptide (Gerber et al, 2003). Right-sided heart failure or complications after pulmonary embolism can accurately be detected by measuring natriuretic peptides, though the cut-off levels were only half of those for left ventricular dysfunction (Kucher et al, 2003). There are two widely accepted area for BNP testing; exclusion of non-cardiac origin of dyspnoe in emergency settings and prognostic information of various states of heart failure. NT-proBNP above 1065 pmol/l had a very high specificity and sensitivity for cardiac failure in our population, similar levels were found in decompensated heart failure, septic shock and acute pulmonary embolism with New York Heart Association III and IV symptoms (Seino et al, 2004). Additionally, lower postoperative cut-off value (513 pmol/l) bore high negative predictive power, indicating a level below which the occurrence of heart failure is unlikely. In these cases, NT-proBNP or BNP measurements are used. Levels above the cut-off level were independently associated with increased risk for mortality and cardiovascular morbidity including cardiac fibrillation. In adults, it has been shown that hyperthyroidism increases the NT-pro BNP level and could reflect cardiac dysfunction secondary to thyreotoxicosis [Kato 2008, Welisch 2011].
ANP or NT-proANP reflect acute changes in atrial wall stress (Ruskoaho, 2003). Therefore, it is not suitable for long-term follow-up of congestive heart failure. Recently, a new immunoassay has been developed for a hybrid peptide (referred to as NT-proXNP) containing peptide sequences from both NT-proANP and NT-proBNP (Ala-Kopsala et al, 2005). This novel assay mimics the physiological signaling pathway since the actions of the different active natriuretic fragments on the target cells are mediated by a single natriuretic peptide receptor. The NT-proXNP assay measures the concentration of the new virtual natriuretic peptide, and thus provides combined information about the plasma levels of NT-proANP and NT-proBNP. In cardiac diseases, the neurohormonal system of the heart is activated. The diagnostic performances of NT-proXNP in adults for coronary artery disease and valvular heart disease are greater than or equal to those of NT-proANP or NT-proBNP, individually. NT-proXNP seems to combine the characteristics of the two natriuretic peptides. Therefore, NT-proXNP will increase earlier during myocardial wall stress than the NT-proBNP alone.



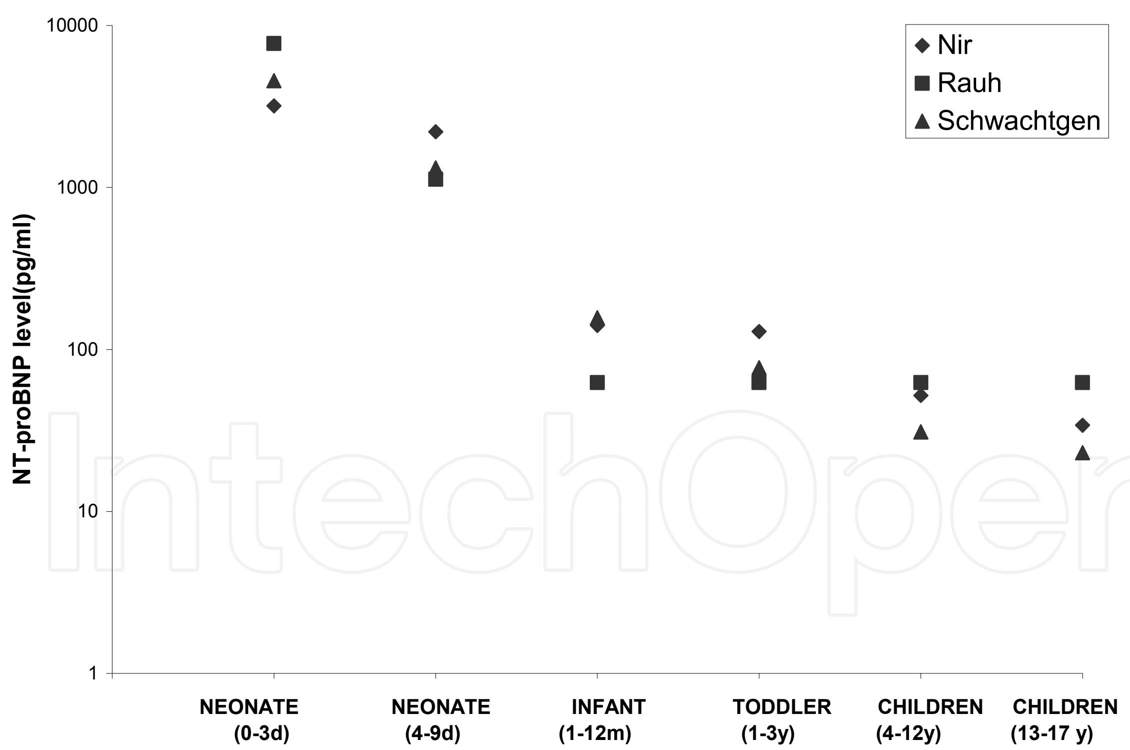


Fig. 1. Refence mean and median values of healthy subjects

3.2 Pediatric population

Based on physiological considerations, BNP and NT-proBNP levels are age dependent in the first two weeks after birth (Albers et al, 2006-Schwachtgen et al, 2005). The perinatal transition from fetal to neonatal circulation is accompanied by an increase in the pulmonary blood flow and an increase in the systemic vascular resistance. These hemodynamic changes lead to pressure and volume load of the heart and it may stimulate the secretion and release of natriuretic peptides. From 31 days to 12 years of age, there is no significant change in healthy subjects (Cantinotti et al, 2010). From 14 years of age, gender related differences should be accounted and it is probably due to steroid sex hormones (Soldin et al, 2006). Age-corrected brain natriuretic peptide and NT-proBNP values should be used in the neonatal population (Cantinotti et al, 2010b), while gender should be considered in the adolescent population. Additionally, it is important to note that reference ranges, decision values are method dependent and it shows variations between the assays and consequently between the studies (Soldin et al, 2006, Cantinotti et al, 2010). These variations are seen in Figure 1. As in the adult population NT-proBNP is significantly higher in children with sepsis. In children with sepsis NT-proBNP levels are higher in some patients with leftventricular dysfunction (Fried 2006). In comparison to the adult population there are no paediatric studies in hyperthyroidism available at present (Welisch 2011).

3.3 Pediatric population – Congenital heart disease

Different requirements have been formulated for the natriuretic peptide assays in the pediatric population. One major area is the exclusion of cardiovascular disease particularly below one year of age. The clinical signs are poor or share the ones with other noncardiac diseases. The major symptoms are dyspnea, tachypnea, cold extremities, murmurs, tachycardia, hypotension, etc. The assay is easy to carry out and requires only 0.5 ml blood. The recent studies showed convincing results that the BNP test could be performed without difficulties from capillary stick and it had a high negative power both in neonates and infants (Law et al, 2009,Maher et al, 2008).
The anatomy of the congenital heart diseases is heterogenous. Additionally, the situation after different types of surgery complicates the hemodynamic state. An arbitrary classification is the following: ventricle volume overload, including left-right shunts, ventricular septal defects, patent ductus arteriosus, atrial septal defect, atrioventricular malformations, truncus arteriosus, etc; pressure overload, as a consequence of outflow tract obstruction or valvular stenosis, such as tetralogy of Fallot, pulmonary or aorta stenosis; univentricular physiology and non-clusterable complex malformations. Despite the age related BNP elevation in the neonatal period, the severity of heart failure can be determined and diagnosed (Cantinotti et al, 2010b, Law et al, 2009). Other studies have been described the linear relationship between BNP or NT-proBNP levels and the magnitude of left-right shunting (Kunii et al, 2003) and BNP levels were able to predict the need for ductus arteriosus closure (Paul et al, 2009). Echocardiographic studies have been confirmed the association between pressure gradient and natriuretic peptide levels (Cowley et al, 2004). In right sided pressure overload, the BNP levels were lower compared to left sided pressure overload (Cantinotti et al, 2009, Holmgren et al, 2005). In Table 1 and 2 pediatric studies measuring BNP and NT-proBNP levels are shown.

3.4 Pediatric cardiac population postoperative period

Monitoring of cardiac output is still a problematic issue, although early recognition of hemodynamic complications is essential in pediatric critical care. During the postoperative period, hemodynamically unstable patients are characterized by high volume intake, the need for considerable inotropic support, edema formation, hepatic congestion, lung

Author	Key words	n	result	Congenital HD	cut-off// lowest level
Lowenthal, A (Lowenthal 2010)	BNP, pediatric Carvedilol trial, heterogenous subject population, cut off values in subgroups	29	positive predictive of heart failure	single ventricle physiology	>30pg/ml
Hall, EK (Hall 2011)	orthotope heart transplantation, follow up, cardiac catheterization, acute cellular rejection	62	Corr betw BNP&right sided pressure measurements	OHT	mean 171pg/ml
Shah A (Shah 2009)	single ventricle, heart failure, BNP	29	Positive predictive of heart failure	single ventricle physiology	>30pg/ml
Cowley C (Cowley 2004)	catherization, BNP correlation pressures espec left ventr outflow obstruction	107	BNP correlates with left ventricular outflow obstruction		median 19pg/ml
Muta H (Muta 2002)	catherization, ASD closure	14	natriuretic peptides may reflect hemodynamic changes	ASD	ANP 24ng/l, BNP23ng/l
Hsu J (Hsu 2007)	neonates, cardiac surgery	36	in neonates BNP predicts poor outcome after cardiac surgery	group 1: stage 1 Norwood,group 2: biventricular repair	
Hsu J (Hsu 2008)	bidirectional cavopulmonary anastomosis, total cavopulmonary connection	36	BNP predicts unplanned surgical/transcatheter interventions includ transplantation	functionally single ventricle	BNP>500pg /ml
Knirsch W (Knirsch 2011)	BNP, PulmHT, AqHD, CongHD	522	BNP useful as follow-up, e.g. BNP decrease after Fontan proc, e.g. BNP decrease after initialization of treatment for PulmHT	yes (heterogeneous group before med treatment,surgery or catherization)	no cut-off values
Berry J (Berry 2008)	single ventricle, prognostic BNP	25	early postoperative BNP levels correlate with ensuing duration of hospitalization and duration of inotropic support	single ventricle to undergo Norwood, Bidirectional cavopulmonary Anastomosis, Fontan	
Law Y (Law 2009)	BNP, rapid triage tool, identify CardVascDisease	100	BNP reliable test to diagnose significant structural or functional CVD in children		BNP: neonatal 170pg/ml, older age 41pg/ml, combined group 44pg/ml
Maher K (Maher 2008)	acute care setting, CongHD, AqHD	103	BNP in acute care settings valuable diagnostic tool	yes, (heterogenous group of 33 children)no	highest median in hypoplastic left heart syndr 4920pg/ml
El-Khuffash, A (El-Khuffash 2011)	PDA, neurodevelopmental outcome, cTNT,preterm	60	possibl assoc cTNT/BNP & hd significant PDA: no statistic significance foud	exclusion criteria	1664vs9209p mol/lNT-proNBNP

Table 1. Usefulness of Brain Natriuretic Peptide measurements. Prospective observational study PO, Brain natriuretic peptide BNP, Atrial natriuretic peptide ANP, cardiac Troponin cTNT, orthotope heart transplantation OHT, persistent Ductus arteriosus PDA, Atria septum defect ASD, pulmonary hypertension pulmHT, aquired heart disease AqHD, congenital heart disease congHD, cardiovascular disease CardVascDis.

Author	Key words	n	Result	Congenital HD	Cut-off// lowest level	Special remarks
Heise G (Heise 2008)	serial, natriuretic hormone system, pulsatile MCS (Berlin Heart EXCOR)	19	serial NP correlate with level of unloading of heart & potential recovery	15 DCM, 2 myocarditis, 1 CongHD, 1 Cardiac arrest in rejection after HTX	250pg/ml on MCS	none
Gessler P (Gessler 2006)	risk stratification for low-risk surgery in CongHD, RACHS-1 score, lactate, duration of CBP, cyanotic defect	40	high NT-proBNP preop predictive of postop prolonged need for inotropic therapy	obstructive lesions/ l-r-shunt/ cyanotic defects		risk stratification for surgery in CongHD
Pietrzak R (Pietrzak 2009)	Fallot correction, rigth ventricular failure, transannular patch, duration of QRS	20	high NT-proBNP may help identify patients at risk for arythmias, rigth ventr failure after Fallot correction	postop correction of Fallot tetralogy	18fmol/l	NT-proBNP higher after TOFl correction
Breuer T (Breuer 2010)	NT-proXNP, neonates/infants <1 year, complete biventriculair repair	26	NT-proXNP correlates with CI	biventriculair repair, <1year	NT-proXNP 3079pmol/l or NT-proBNP 2051pmol/l ~CI<3l/min/m2	none
Kaneko K (Kaneko 2011)	kawasaki syndrome,NT-proBNP, coronary arterial lesions	43	risk to develop coronary artery lesions 10x higher with NT-proBNP>1000pg/ml		NT-proBNP>1000pg/ml	none
Joseph L (Joseph 2010)	Bronchopulmonarydysplasia,natriureticpeptides,prematurity <34weeks gest	34	NT-proBNP signif higher with BPD, NT-signif higher with Resp Distress Syndr	Cong HD/ sepis/ current PDA exclusion criteria		none
Mazurek B (2009)	idiopathic ventricular arrhythmia, asymptomatic circulatory failure	36	NT-proBNPincreases with malignant ventricular arrhythmia	none,idiopathic ventricular arrhythmia	66pg/ml median in group malign arryhthmia	none
Rusconi P (Rusconi 2010)	dilated cardiomyopathy (idiopathic, anthracycline-related, uremic, muscular dystrophy), heart failure, changes in echocardiographic evalutaion of HF	36	serial NT-proBNP >1000pg/ml correlates with HF, echodardiographic measures correlate with NT-proBNP changes within patients	none	NT-proBNP>1000pg/ml; NT-proBNP <450pg/ml asymptomatic patients;	retrospective ;NT-proBNP <450pg/ml
Nir A (Nir 2009)	reference values neonates/infants, log-normal distribution, high NT-proBNP in pubertal girls	690	reference values for pediatr population	no, no cardiac disease, no respiratory disease	see table 1	combined study data
Cohen S (Cohen 2005)	differenciate between cardiac or respiratory problem	48	BNP differentiates between heart failure and lung disease, BNP for monitoring treatment for heart failure	yes (heterogeneous group)	2940pg/ml	none

Author	Key words	n	Result	Congenital HD	Cut-off// lowest level	Special remarks
Mir T (Mir 2002)	establish normal age-related NT-proBNP levels in children form infant to adulthood, compare CongestiveHF with controlgrou	164	NT-proBNP is higher in children with CHF, correlates with severity of clinical signs and echocardiographic EF	yes, (heterogenous group of 31 children)	no	none
Wong D (Wong 2011)	mechanical circulatory support, transplantation, acute decompensated heart failure	24	signif diff MCS/no-MCS, but not predictive	4 CHD, 17 cardiomyopathy, 3 "other"	Median of max value 40pg/ml	none

Table 2. Usefulness of NT-proBrain Natriuretic Peptide measurements. Retrospective study r, n-terminal pro-brainnatriureticpeptide NT pro-BNP, brain natriuretic peptide BNP, dilated cardiomyopathy DCM, congestive heart failure congestiveHF, mechanical circulatory support MCS; cardiopulmonary bypass CPB, total corretion of Fallot TOF, persistent Ductus arteriosus PDA, Risk Adjustement for Congenital Heart Surgery RACHS-1 (Jenkins 2004)

dysfunction or the combination of them (Laussen & Roth, 2003). High lactate levels and low base excess on the first postoperative day have been reported to predict mortality and outcome in pediatric cardiac patients (Tibby et al, 1999, Carmona et al, 2008). Mir et al.found limited value of NT-proBNP levels in the perioperative period. In their study, dosage and duration of catecholamines and length of mechanical ventilation correlated with postoperative troponin T and arterial lactate levels, but not with NT-proBNP (Mir et al, 2006). Since catecholamine therapy is a consequence of hemodynamic instability and prolonged mechanical ventilation can be influenced by certain non-cardiac factors, the direct relationship might be concerned. Indeed, clinical signs and scores of congestive heart failure is difficult to apply as diaphoresis, respiratory rate, heart rate in the early postoperative period are strongly modified by inotropic, analgesic and sedative medication (Tibby et al, 1999). Preoperative NT-proBNP was associated with adverse postoperative outcome in children undergoing heart surgery, like duration of mechanical ventilation, dose of inotropic support, length of intensive care unit stay (33-Hsu et al, 2007). BNP and NT-proBNP levels usually exceed the peak maximum at 12 hours, and a second peak may occur about five days after surgery (Koch et al, 2007). Postoperative BNP and NT-proBNP levels have also been shown to have prognostic value after pediatric cardiac surgery. After cavopulmonary anastomosis a decrease in natriuretic peptides level compared to preoperative level were correlated with better outcomes (Hsu et al, 2008). Prognostic role of BNP was also reported after switch surgery in neonates (Lehot et al, 1992).

Our study investigated the prognostic role of NT-proXNP, a hybride analyte. NT-proXNP level correlated significantly with the simultaneously measured NT-proANP level ($r = 0.60$, $p < 0.001$), but more strongly with NT-proBNP level ($r = 0.89$, $p < 0.001$) and the arithmetic sum of both peptides throughout the perioperative period ($r = 0.88$, $p < 0.001$). Baseline NT-proXNP level correlated with the age ($r = -0.72$, $p < 0.001$) and the weight of the patients ($r = -0.47$, $p = 0.026$). Preoperative creatinine level (53.3 ± 13.1 μmol/l) correlated with baseline NT-proXNP ($r = 0.53$, $p = 0.013$). The duration of operation and the duration of CPB were associated with the preoperative NT-proXNP level ($r = 0.58$, $p = 0.005$ and $r = 0.62$ $p = 0.002$,

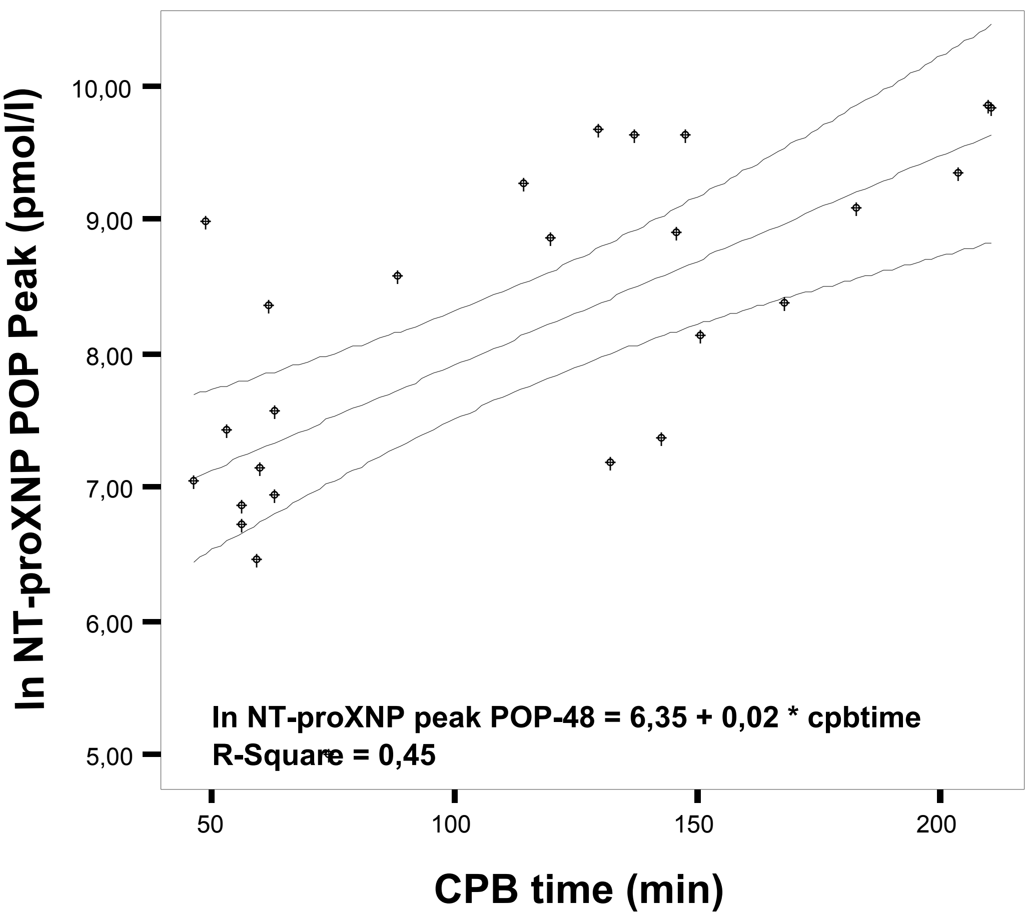


Fig. 2. Correlation between logarithmic transformed NT-proXNP levels and cardiopulmonary bypass time

respectively) and the peak postoperative NT-proXNP level (r = 0.64, p < 0.001 and r = 0.67, p < 0.001, respectively). NT-proBNP showed similar correlations with the duration of operation and CPB (Breuer et al, 2010). In the postoperative period, natriuretic peptide levels correlated significantly with the simultaneously assessed hemodynamic parameters. NT-proXNP correlated stronger with the hemodynamic parameters except for extravascular lung water index than the arithmetic sum of NT-proANP and NT-proBNP. The correlation between NT-proXNP and CI remained significant after adjusting for age (r = 0.60, p = 0.018) or weight (r = 0.81, p < 0.001).

The hemodynamic parameters improved during the postoperative period as the myocardium recovered. The application of transpulmonary thermodilution was safe and reliable and it added useful information to the conventionally measured pressure values in neonates and infant following open heart surgery. We found lower global enddiastolic volume indices and higher extravascular lung water indices compared to adult ranges, whereas the cardiac indices were the same. Age related and disease specific reference values of the transpulmonary thermodilution parameters are yet to be determined in children.

In ROC analysis, a postoperative NT-proBNP level of 2051 pmol/l was diagnostic for cardiac index (CI) lower than 3 l/min/m2 with 79% sensitivity and 95% specificity (AUC: 0.87 ± 0.06), whereas a postoperative NT-proXNP level of 079 pmol/l was diagnostic for that with 89% sensitivity and 90% specificity (AUC: 0.91 ± 0.05). The length of mechanical ventilation and ICU stay did not correlate with the baseline or the peak natriuretic peptide levels. NT-proBNP and NT-proXNP, but not NT-proANP level at 24 hours after surgery were correlated to the length of mechanical ventilation (r = 0.51, p = 0.015 and r = 0.47, p = 0.027, respectively). The area under the curve (AUC) of NT-proBNP and NT-proXNP at 24 hours after surgery for prolonged mechanical ventilation (> 72h) in ROC analysis was 0.81 ± 0.10 and 0.72 ± 0.11, respectively.

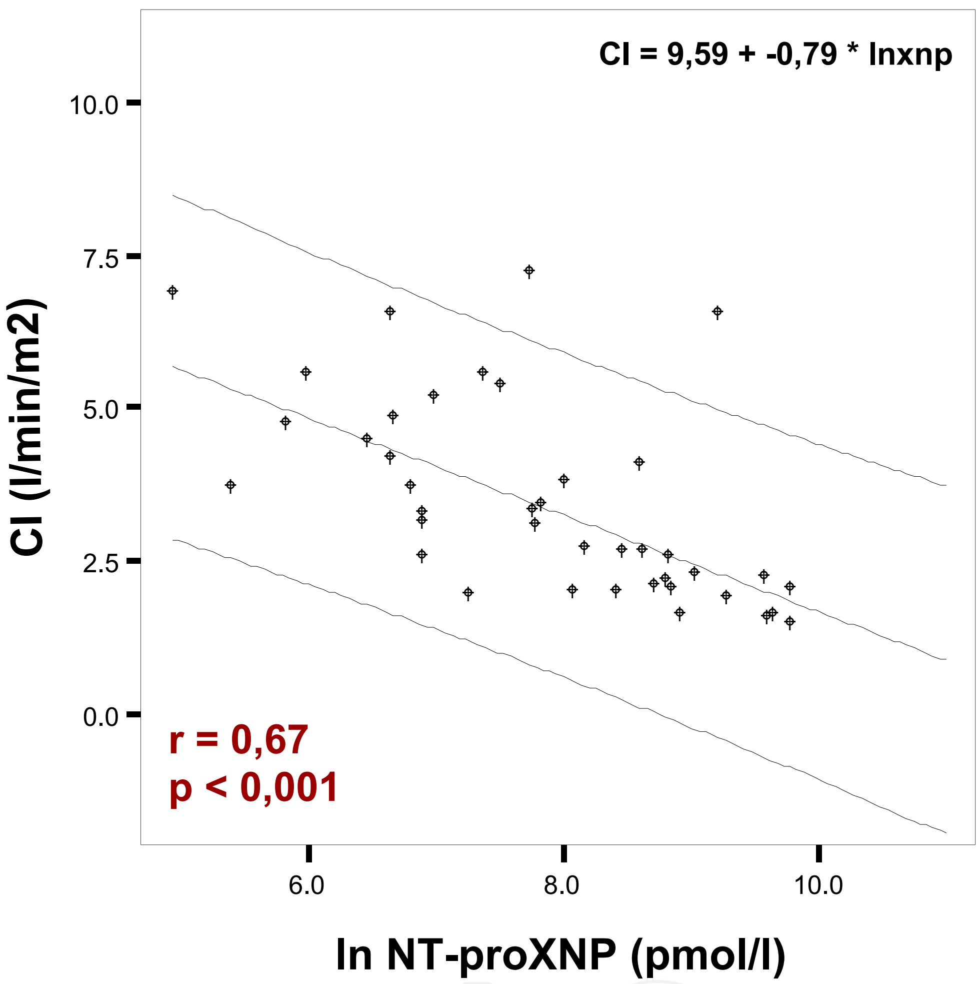


Fig. 3. Relationship between logarithmic transformed NT-proXNP levels and Cardiac index

Conventionally measured parameters such as heart rate, mean arterial pressure and pulse-pressure product exhibited weaker correlations with CI than natriuretic peptide levels. Parameters measured by echocardiography i.e. fractional shortening and calculated pressures of the right ventricle were not correlated to CI. Clinical and laboratory values, except for creatinine level and creatinine clearance, showed no correlation with CI or NT-proXNP. According to our findings, natriuretic peptides and NT-proXNP are indicators of hemodynamic parameters following pediatric cardiac surgery that can only be measured by invasive hemodynamic monitoring.

3.5 Pediatric cardiac population–follow-up period

Pediatric cardiac population follow-up period Pediatric patients with simple cardiac lesions after corrective surgery show a marked reduction in BNP and NT-proBNP levels compared to the preoperative period. The same is true after catheter interventions, like closure of atrial septal defect or closure of ductus arteriosus. In patients with residual defects, like pulmonary stenosis or pulmonary arterial hypertension, serial measurements of BNP or NT-proBNP levels provide a useful, easy and non-invasive tool for follow-up and it can be used for quantification of the disease severity. During the follow-up of cardiac transplant patients rejection can be detected by increase of BNP levels.

4. Conclusion

Natriuretic peptide levels are age dependent and show significant variability according to the type of the cardiac malformation and the actual hemodynamic condition. Recently, age related normal values have been established in the neonatal period and it allows detection of the congental heart disease in different age groups. Right sided hemodynamic ventricular stress is encountered with lower BNP values. Preoperative and postoperative application of natriuretic peptides provides a useful tool for the detection of postoperative complications. The new analyte, NT-proXNP seems to have promising characteristics, because it reflects the cardiac output changes earlier than the BNP, NT-proBNP assay.

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6. References

Ala-Kopsala M, Ruskoaho H, Leppaluoto J, Seres L, Skoumal R, Tóth M, Horkay F, Vuolteenaho O. (2005) Single assay for amino-terminal fragments of cardiac A- and B-type natriuretic peptides. *Clin Chem* Vol 51 pp 708-18.

Albers S, Mir TS, Hada M, Laer S. (2006)N-terminal probrain natriuretic peptide: normal ranges in the pediatric population including method comparison and interlaboratory variability. *Clin Chem Lab Med* Vol.44 pp 80-85.

Baumgartner H, Bonhoeffer P, De Groot NM, de Haan F, Deanfield JE, Galie N, et al. (2010) ESC Guidelines for the management of grown-up congenital heart disease (new version 2010): the Task Force on the Management of Grown-up Congenital Heart Disease of the European Society of Cardiology (ESC). *Eur Heart J* Vol;31 pp 2915–57.

Berry JG, Askovich B,.Shaddy A, Hawkins J, Cowley CG (2008) Prognostic Value of B-Type Natriuretic Peptide in Surgical Palliation of Children with Single-Ventricle Congenital Heart Disease. *PediatrCardiol*, Vol 29 pp 70–75

Breuer T, Sápi E, Skoumal R, Tóth M, Ala-Kopsala M, Vuolteenaho O, Leppäluoto J, Ruskoaho H, Szatmári A, Székely A. (2007) N-terminal pro-brain natriuretic peptide level inversely correlates with cardiac index after arterial switch operation in neonates. *Pediatric Anesthesia* Vol 17 pp 782-8..

Breuer T, Skoumal R, Horkay F, Merkely B, Ala-Kopsala M, Leppäluoto J, Vuolteenaho O, Ruskoaho H, Tóth M., Székely A. (2010)Strong relationship between NT-proXNP levels and cardiac output following cardiac surgery in neonates and infants. *Acta Anaesthesiologica Scandinavica*; Vol 54 pp 502-9.

Cantinotti M, Vittorini S, Storti S, Prontera C, Murzi M, De Lucia V, et al.(2009) Diagnostic accuracy and clinical relevance of brain natriuretic peptide assay in pediatric patients with congenital heart diseases. J Cardiovasc Med (Hagerstown) Vol 10 pp 706–13

Cantinotti M, Storti S, Parri MS, Prontera C, Murzi B, Clerico A.(2010)Reference intervals for brain natriuretic peptide in healthy newborns and infants measured with an automated immunoassay platform. Clin Chem Lab Med; Vol 48 pp 697–700.

Cantinotti M, Storti S, Ripoli A, Zyw L, Crocetti M, Assanta N, et al. (2010) Diagnostic accuracy of B-type natriuretic hormone for congenital heart disease in the first month of life. Clin Chem Lab Med Vol 48 pp 1333–8.

Cantinotti M, Giovannini S, Murzi B, Clerico A (2011) Diagnostic, prognostic and therapeutic relevance of B-type natriuretic hormone and related peptides in children with congenital heart diseases. *Clin Chem Lab Med*, Vol 49 pp 567-580

Carmona F, Manso PH, Vicente WV, Castro M, Carlotti AP (2008). Risk stratification in neonates and infants submitted to cardiac surgery with cardiopulmonary bypass: a multimarker approach combining inflammatory mediators, N-terminal pro-B-type natriuretic peptide and troponin I. *Cytokine*; Vol 42 pp 317-24.

Clerico A, Recchia FA, Passino C, Emdin M. (2006) Cardiac endocrine function is an essential component of the homeostatic regulation network: physiological and clinical implications. Am J Physiol Heart Circ Physiol; Vol 290 pp H17–29.

Cohen S, Springer C, Avital A, Perles Z, Rein A, Argaman Z, Nir A (2005) Amino-Terminal Pro-Brain-Type Natriuretic Peptide: Heart or Lung Disease in Pediatric Respiratory Distress? *Pediatrics*, Vol 115 pp 1347–1350;

Costello JM, Backer CL, Checchia PA, Mavroudis C, Seipelt RG, Goodman DM. (2005) Effect of cardiopulmonary bypass and surgical intervention on the natriuretic hormone system in children. *J Thorac Cardiovasc Surg*; Vol 130 pp 822-9.

Cowley CG, Bradley JD, Shaddy RE.(2004) B-type natriuretic peptide levels in congenital heart disease. *Pediatr Cardiol*; Vol 25: 336-40.

de Lemos JA, Morrow DA, Bentley JH, et al. (2001) The prognostic value of B-type natriuretic peptide in patients with acute coronary syndromes. N Engl J Med Vol 345 pp 1014– 21.

El-Khuffash A, Slevin M, McNamara P, Molloy EJ (2011) Troponin T, N-terminal pro natriuretic peptide and a patent ductus arteriosus scoring system predict death before discharge or neurodevelopmental outcome at 2 years in preterm infants. *Arch Dis Child Fetal Neonatal Ed*, Vol 96 pp F133–F137

Fried I, Bar-Oz B, Algur N, Fried E, Gavri S, Yatsiv I, Perles Z, Rein A, Zonis Z, Bass R, Nir A (2006) Comparison of N-terminal Pro-B-Type Natriuretic Peptide Levels in Critically Ill Children With Sepsis Versus Acute Left Ventricular Dysfunction. *Pediatrics*, Vol 118 pp e1165

Gerber IL, Stewart PAH, Legget ME, et al (2003) Increased plasma natriuretic peptide levels reflects symptom onset in aortic stenosis. *Circulation*; Vol 107 pp 1884-1890.

Gessler P, Knirsch W, Schmitt B, Russon V, von Eckardstein A (2006) Prognostic value of plasma N-Terminal pro-Brainnatriureticpeptide in children with congenital heart defects and open-heart surgery. *J Pediatr*, Vol 148 pp 372-376

Hall EK, Glatz AC, Quartermain DM, Ravishankar C, Kaufman B, Cohen M, Hanna BD, Goldberg JD (2011) Brain-type natriuretic peptide correlates with right heart pressures in a cross section of pediatric heart transplant patients. *Pediatr Transplant*, Vol 15 pp70-74

Hama N, Itoh H, Shirakami G, Nakagawa O, Suga S, Ogawa Y, Masuda I, Nakanishi K, Yoshimasa T, Hashimoto Y, Yamaguchi M, Hori R, Yasue H, Nakao K. (1995) Rapid ventricular induction of brain natriuretic peptide gene expression in experimental acute myocardial infarction. Circulation; Vol 92 pp 1558-64.

Heise G, Lemmer J, Hübler M, Weng Y, Alexi-Meskishvili V, Böttcher W, Hetzer R, Berger F, Stiller B (2008) Biomarker Responses During Mid-term Mechanical Cardiac Support in Children. *J Heart Lung Transplant*, Vol 27 pp 150–7

Holmgren D, Westerlind A, Lundberg PA, Wåhlander H. (2005) Increased plasma levels of natriuretic peptide type B and A in children with congenital heart defects with left compared with right ventricular volume overload or pressure overload. *Clin Physiol Funct Imaging*; Vol 25 pp 263-9.

Hsu JH, Keller RL, Chikovani O, Cheng H, Hollander SA, Karl TR, Azakie A, Adatia I, Oishi P, Fineman JR. (2007) B-type natriuretic peptide levels predict outcome after neonatal cardiac surgery. *J Thorac Cardiovasc Surg*; Vol 134 pp 939-45.

Hsu JH, Oishi PE, Keller RL, Chikovani O, Karl TR, Azakie A, et al. (2008) Perioperative B-type natriuretic peptide levels predict outcome after bidirectional cavopulmonary anastomosis and total cavopulmonary connection. J Thorac Cardiovasc Surg; Vol 135 pp 746–53

Jenkins KJ (2004) Risk adjustement for congenital heart surgery: the RACHS-1 method. Sem Thorac Cardiovas Surg Pediatr Card Surg Annu, Vol 7 pp 180-184

Joseph L, Nir A, Hammerman C, Goldberg S, Shalom EB, Picard E (2010)N-terminal pro-B-type Natriuretic Peptide as a Marker of Bronchopulmonary Dysplasia in Premature Infants. *Am J Perinatol*, Vol 27 pp 381–386

Kaneko K, Yoshimura K, Ohashi A, Kimata T, Shimo T, Tsuji S (2011) Prediction of the Risk of Coronary Arterial Lesions in Kawasaki Disease by Brain Natriuretic Peptide. *Pediatr Cardiol*, DOI10.1007/s00246-011-9986-8

Kangawa K, Fukuda A, Kubota I, Hayashi Y, Minamitake Y, Matsuo H. (1984)Human atrial natriuretic polypeptides (hANP): purification, structure synthesis and biological activity. J Hypertens Suppl; Vol 2 pp S321-3.

Kato K, Murakimo H, Isozaki O Endocrine J, Thushima T, Takano K (2009) Serum Concentrations of BNP and ANP in patients with thyreotoxicosis. *Endocrine J*, Vol 56 pp 17-27

Knirsch W, Häusermann E, Fasnacht M, Hersberger M, Gessler P, Bauersfeld U (2011) PlasmaB-type natriuretic peptide levels in children with heart disease. ActaPædiatrica ISSN0803–5253

Koch A, Singer M. Normal values of B type natriuretic peptide in infants, children, and adolescents. (2003) *Heart*; Vol 89 pp 875–8.

Koch A, Kitzsteiner T, Zink S, Cesnjevar R, Singer H. Impact of cardiac surgery on plasma levels of B-type natriuretic peptide in children with congenital heart disease (2007). Int J Cardiol; Vol 114 pp 339–44.

Kucher N, Printzen G, Goldhaber SZ. (2003) Prognostic role of brain natriuretic peptide in acute pulmonary embolism. Circulation; Vol 107 pp 2545–2547.

Kunii Y, Kamada M, Ohtsuki S, Araki T, Kataoka K, Kageyama M. (2003) Plasma brain natriuretic peptide and the evaluation of volume overload in infants and children with congenital heart disease. Acta Med Okayama; Vol 57 pp 191–7

Laussen PC, Roth SJ. Fast tracking: efficiently and safely moving patients through the intensive care unit. (2003) *Prog Pediatr Card*; Vol 18 pp 149-158.

Law Y.M., Hoyer A.W., Reller M.D. and Silberbach M., Accuracy of plasma B-type natriuretic peptide to diagnose significant cardiovascular disease in children: the better not pout children! Study (2009), *J Am Coll Cardiol*; Vol 54: pp 1467–1475

Lehot JJ, Villard J, Piriz H, Philbin DM, Carry PY, Gauquelin G, Claustrat B, Sassolas G, Galliot J, Estanove S. (1992) Hemodynamic and hormonal responses to hypothermic and normothermic cardiopulmonary bypass. *J Cardiothorac Vasc Anesth*; Vol 6 pp 132-9.

Lindahl B, Toss H, Siegbahn A, et al. for the FRISC Study Group. (2000) Markers of myocardial damage and inflammation in relation to long-term mortality in unstable coronary artery disease. *N Eng J Med*; Vol 343 pp 1139-1147.

Lowenthal A, Shah A, Bernstein H (2010) Letter by Lowenthal et al Regarding Article,"BNP Levels Predict Outcome in Pediatric Heart Failure Patients: Post Hoc Analysis of the Pediatric Carvedilol Trial". *Circ Heart Fail*, Vol 3: pp e32

Maher KO, Reed H, Cuadrado A, et al. (2008) B-type natriuretic peptide in the emergency diagnosis of critical heart disease in children. *Pediatrics*; Vol 121: pp e1484–8.

Maisel AS, Krishnaswamy P, Nowak RM, et al. (2002) Rapid measurement of B-type natriuretic peptide in the emergency diagnosis of heart failure. *N Eng J Med*; Vol 347 pp 161-167.

Mazurek B, Szydłowski L, Giec-Fuglewicz G, Markiewicz-ŁoskoG (2009) N-terminal Prohormone Brain Natriuretic Peptide-pro BNP Levels in Ventricular Arrhythmias in Children. *Clin.Cardiol*, Vol 32 pp 690–694

Mir TS , Marohn S, Läer S, Eiselt M, Grollmus O, Weil J (2002) Plasma Concentrations of N-Terminal Pro-Brain Natriuretic Peptide in Control Children From the Neonatal to Adolescent Period and in Children With Congestive Heart Failure. *Pediatrics*, Vol 110(6) pp e76.

Mir TS, Haun C, Lilje C, et al. (2006) Utility of N-Terminal Brain Natriuretic Peptide Plasma Concentrations in Comparison to Lactate and Troponin in Children with Congenital Heart Disease Following Open-Heart Surgery. *Pediatr Cardiol*. Vol 27 pp 209-216.

Muta H, Ishii M, Maeno Y, Akagi T, Kato H (2002) Quantitative evaluation of the changes in plasma concentrations of cardiac natriuretic peptide before and after transcatheter closure of atrial septal defect. *Acta Pediatr*, Vol 91 pp 649 652

Nir A, Lindinger A, Rauh M, Bar-Oz B, Laer S, Schwachtgen L, et al. (2009) NT-Pro-B-type natriuretic peptide in infants and children: reference values based on combined data from four studies. *Pediatr Cardiol* Vol 30 pp 3–8.

Paul MA, Backer CL, Binns HJ, Mavroudis C, Webb CL, Yogev R, et al. (2009) B-type natriuretic peptide and heart failure in patients with ventricular septal defect: a pilot study. *Pediatr Cardiol* Vol 30 pp 1094–7

Pietrzak R, Werner B (2009) Usefulness of NT-proBNP in assessment of right ventricular function in children after tetralogy of Fallot correction –apreliminary study. *Kardiol Pol*, Vol 67 pp 378-383

Rauh M, Koch A. (2003) Plasma N-terminal pro-B-type natriuretic peptide concentrations in a control population of infants and children. *Clin Chem*; Vol 49 pp 1563–4.

Ruskoaho H. Cardiac hormones as diagnostic tools in heart failure. (2003) *Endocr Rev* Vol 24 pp 341-56.

Ruskoni P, Ludwig D, Ratnasamy C, Masa R, Harmon WG, Colan SD, Lipshultz S (2010) Serial measurements of serum NT-proBNP as markers of left ventricular systolic function and remodeling in children with heart failure. *Am Heart J*, Vol 160 pp 776-83

Schwachtgen L, Herrmann M, Georg T, Schwarz P, Marx N, Lindinger A (2005). Reference values of NT-proBNP serum concentrations in the umbilical cord blood and in healthy neonates and children. *Z Kardiol* Vol;94 pp 399–404.

Seino Y, Ogawa A, Yasamita T, et al. (2004) Application of NT-proBNP and BNP measurements in cardiac care: a more discerning marker for detection and evaluation of heart failre. *Eur J Heart Fail* ; Vol 6 pp 295-300

Shah A, Feraco AD, Harmon C, Tacy T, Fineman JR, Bernstein HS (2009) Usefulness of Various Plasma Biomarkers for Diagnosis of Heart Failure in Children with Single Ventricle Physiology. *Am J Cardiol*, Vol 104 pp 1280-1284

Shih CY, Sapru A, Oishi P, Azakie A, Karl TR, Harmon C, Asija R, Adatia I, Fineman JR. (2006) Alterations in plasma B-type natriuretic peptide levels after repair of congenital heart defects: a potential perioperative marker. *J Thorac Cardiovasc Surg*; Vol 131 pp 632-8.

Silberbach M, Roberts CT Jr. (2001) Natriuretic peptide signaling: molecular and cellular pathways to growth regulation. *Cell Signal*; Vol 13 pp 221-31.

Soldin SJ, Soldin OP, Boyajian AJ, Taskier MS. (2006) Pediatric brain natriuretic peptide and N-terminal pro-brain natriuretic peptide reference intervals. *Clinica Chimica Acta*; Vol 366 pp 304-308.

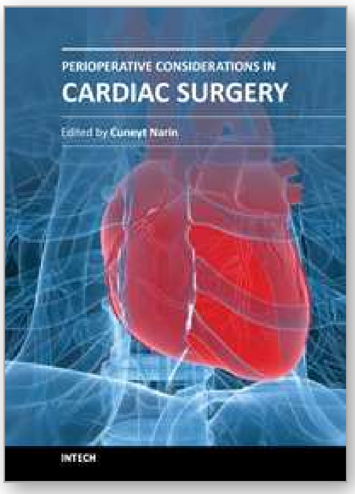
Székely A, Breuer T, Sápi E, Székely E, Szatmári A, Tóth M, Hauser B, Gál J. (2010) Transpulmonary thermodilution in neonates undergoing arterial switch surgery. *Pediatric Cardiology*; Vol 32(2) pp 125-30

Tibby SM, Hatherill M, Murdoch IA. (1999) Capillary refill and core-peripheral temperature gap as indicators of haemodynamic status in paediatric intensive care patients. *Arch Dis Child*; Vol 80 pp 163-6.

Tobias JD (2011) B-type Natriuretic Peptide: Diagnostic and Therapeutic Applications in Infants and Children. *J Intensive Care Med*, Vol 26: pp 183-195

Welisch E, Norozi K, Rauch R (2011) N-terminal pro-brain natriuretic peptide level as a screening tool for cardiac involvement in paediatric diseases of extra cardiac origin. *Clin Res Cardiol*, DOI10.1007/s00392-011-0317-0

Wong D, George K, Wilson J, Manlhiot C, McCrindle BW, Adeli K, Kantor PF (2011) Effectiveness of Serial Increases in Amino-Terminal Pro–B-Type Natriuretic Peptide Levels to Indicate the Need for Mechanical Circulatory Support in Children With Acute Decompensated Heart Failure. *Am J Cardiol*, Vol 107 pp 573–578



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This book considers mainly the current perioperative care, as well as progresses in new cardiac surgery technologies. Perioperative strategies and new technologies in the field of cardiac surgery will continue to contribute to improvements in postoperative outcomes and enable the cardiac surgical society to optimize surgical procedures. This book should prove to be a useful reference for trainees, senior surgeons and nurses in cardiac surgery, as well as anesthesiologists, perfusionists, and all the related health care workers who are involved in taking care of patients with heart disease which require surgical therapy. I hope these internationally cumulative and diligent efforts will provide patients undergoing cardiac surgery with meticulous perioperative care methods.

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