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Original Article

Predictive Value of Post-operative Cardiac Troponin I and Lactate Levels After Ventricular Septal Defect Closure

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Abstract

Objectives: Although the mortality rate of primary ventricular septal defect (VSD) closure surgery has been reduced to <0.5% in many centers, low cardiac output syndrome and multi-organ failure syndrome development in the post-operative period are still the most common causes of mortality and morbidity. The use of biochemical markers in the early period can be used as effective predictors for reducing mortality and morbidity. In this study, the effect of post-operative serum lactate and cardiac troponin I (cTNI) levels on hospital mortality in patients who underwent primary closure of VSD was investigated retrospectively.

Methods: The effect of lactate and cTNI values on hospital mortality in 52 patients who underwent surgical repair for VSD was investigated. Serum lactate levels of all patients in the first 6 h after the operation; on the first post-operative day, cTNI values were examined retrospectively. Serum lactate levels exceeding 3.5 mmol/lt and cTNI values exceeding 35 ng/mL were determined as the cut-off points.

Results: Serum lactate level and cTNI increase were found to be statistically different in the mortality group ($p<0.05$). It was shown that increased cTNI was associated with weight, left ventricular end-diastolic diameter, and cardiopulmonary bypass time ($p<0.05$). Serum lactate levels were 4.1±0.5 mmol/lt in the non-mortality group and 15.3±8.3 mmol/lt in the mortality group, and the difference was statistically significant ($p<0.05$). Hospital mortality was observed in 6 patients.

Conclusion: In patients undergoing VSD closure surgery, serum lactate levels measured in the first 6 h post-operatively and cTNI levels measured on the first post-operative day are associated with hospital mortality. Concomitant elevations of lactate and cTNI values in patients after VSD closure should suggest to take caution and early supportive treatments to reduce mortality.

Keywords: cTNI; hospital mortality; serum lactate level; VSD.

Postoperatif Kardiyak Troponin I , Serum Laktat Seviyelerinin Ventriküler Septal Defekt Operasyonu Sonrası Prediktif Etkisi

Özet

Amaç: Bir çok merkezde primer ventriküler septal defekt(VSD) kapatılması operasyonunun mortalitesi %0,5 'lerin altına düşürülsede postoperatif dönemde düşük kardiyak debi (LCOS) ve multi organ yetmezlik sendromu (MOYS) gelişimi halen en sık mortalite ve morbidite sebebi olarak izlenmektedir. Erken dönemde biyokimyasal belirteçlerin kullanılması mortalite ve morbiditenin azaltılmasında etkin prediktörler olarak kullanılabilir. Bu çalışmada, ventriküler septal defekt (VSD) primer kapatılması operasyonu geçirmiş hastaların postoperatif serum laktat, kardiyak troponin I (cTNI), düzeylerinin hastane mortalitesine etkisi geriye dönük olarak araştırıldı.

Gereç ve Yöntem: VSD'nin cerrahi tamiri yapılan 52 hastanın laktat ve kardiyak troponin değerlerinin hastane mortlitesine etkisi araştırıldı. Tüm hastaların operasyon sonrası ilk 6 saatlik dönemde serum laktat; postoperatif birinci günde ise cTNI değerleri geriye dönük olarak incelendi. Serum laktat seviyesinin 3,5 mmol/lt, cTNI değerinin 35 ng/ml üzerine çıkması sınır değer olarak belirlendi.

This study was presented as an online oral presentation at the 43th Pediatrics Days (30 May-2 July 2021).

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Bulgular: Mortalite üzerinde serum laktat seviyesi ve cTNI artışı istatistiksel olarak anlamlı bulundu (p<0,05). cTNI artışıyla operasyon kilosunun, sol ventrikül diastol sonu çapının (LVEDD) ve kardiyopulmoner baypass (KPB) süresinin ilişkili olduğu gösterildi (p<0,05). Serum laktat seviyeleri sağ kalan grupta ortalama 4,1±0,5 mmol/lt, mortalite gelişen grupta 15,3±8,3 mmol/lt idi ve istatistiksel olarak fark anlamlı izlendi (p<0,05) . Hastaların 6'sında hastane mortalitesi izlendi.

Sonuç: VSD kapatılması operasyonu geçiren hastalarda postoperatif ilk 6 saatte bakılan serum laktat seviyeleri, postoperatif 1. gün bakılan cTNI düzeyleri hastane mortalitesiyle ilişkilidir. Yüksek laktate ve cTNI düzeyi olan ameliyat olmuş VSD hastalarında erken tedaviler başlanmalıdır.

Anahtar sözcükler: cTNI; hastane mortalitesi; serum laktat seviyesi; ventriküler septal defekt.

Introduction

In the last three decades, mortality and morbidity rates following ventricular septal defect (VSD) repair have decreased significantly. Mortality rates in the Society of Thoracic Surgeons database range between 0.3 and 0.7%.[1] However, in developing countries, VSD may be deleterious because of late admission.[2] The most common cause of early post-operative mortality in pediatric cardiac surgery is low cardiac output syndrome (LCOS), which develops after the surgery.[3–5] LCOS is deteriorated systemic perfusion due to myocardial dysfunction.[6] The use of biochemical markers such as serum lactate levels and cardiac troponin I (cTNI) levels in intensive care follow-up can be used as predictors of early mortality.

cTNI is a biomarker with high specificity and sensitivity for indicating myocardial ischemia and damage. It is used as the most important marker of myocardial deterioration in adult patients. In pediatric patient groups, high lactate levels in the intensive care unit are an important early indicator of LCOS and an important indicator of hospital mortality. In this study, post-operative serum lactate levels and cTNI levels were retrospectively investigated concerning hospital mortality in patients who underwent VSD closure.

Materials and Methods

Patients who underwent surgical VSD closure between 2011 and 2013 were examined. In addition to VSD, other cardiac anomalies contaminated with VSD, Atrial septal defect (ASD), and patent ductus arteriosus (PDA), were included in the study.

To conduct this study, the issue was discussed with the institutional ethics committee, and approval was received for the research (February 01, 2013-issue number 300).

Demographic data, pre-operative echocardiography, and catheter reports of 52 patients who met the acceptance criteria were examined. VSD types, sizes, cardiac anomalies in addition to VSD, left ventricule ejection fracture (LVEF, %) values, left and right ventricular end-diastolic diameters (LVEDD, RVEDD), mean pulmonary arterial pressures (MPAP), and systemic to pulmonary flows ratio (Qp/Qs) were obtained from records. Post-operative day 0 was considered the day of the operation, and post-operative day 1 was the day after surgery.

As intraoperative data, cross-clamp times, the need for repeat cross-clamping, and cardiopulmonary bypass (CPB) time were also examined.

Serum lactate values in the patients during the 1st day in the intensive care unit (ICU) were regularly (6-h interval) examined, and the post-operative 6th h value was taken into the study. cTNI values taken upon arrival at the ICU and on the morning of the 1st day were recorded. Post-operative inotropic supports, ICU stay, hospital stay, and 30-day hospital mortality were checked.

Statistical Analysis

All data were transferred to SPSS 21 (IBM Corp., Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY). Statistical data: mean values are expressed as standard errors and percentages where appropriate. The chi-square test and t-test were used to compare the values. A probability value (p) below 0.05 was considered significant. The confidence interval was determined to be 95%.

Results

Pre-operative Data

Twenty-six (50%) of the 52 patients were female. The mean age was 34.6±8.5 months. According to the Anderson VSD classification,[7] perimembranous defects were observed in 86.5% of the patients; 5.8% of patients have muscular type VSD; double-committed juxta arterial at 3.8%; and combined types at 3.8%. ASD was present in 30 (57.8%) patients and PDA in 8 (15.4%) patients. One (1.9%) patient had previously undergone balloon dilatation due to aortic coarctation. AVP was found in twenty-eight (53.8%) patients.

Post-operative Course

Post-operative arrhythmia was observed in 17 patients. One patient had a permanent heart block and underwent pacemaker implantation. Twelve patients had junctional ectopic arrhythmia. Inotropic support for more than 6 h is classified only as dopamine (n=21), dopamine, or dobutamine with adrenaline (n=13). Twelve patients received inotropic support for no or <6 h.

Analysis of Data According to the Mortality

Mortality was observed in 6 patients. The mean age (months) in the mortality group was 48.6±7.3 and 32.5±9.4 in the non-mortality group (p=0.39). Three of the six patients had trisomy 21. There was no significant difference in pulmonary and systemic flow rates (Qp/Qs) between the two groups (mortality group 2.51±0.16, non-mortality group 2.61±0.65; p>0.05).

In the MPAP (mmHg) examination, the pressures were found to be 42±2.2 mmHg in the mortality group, while they were

Table 1. Analysis of data according to the mortality

Variable	Mortality group Mean±SE	Non-mortality group Mean±SE	p
Age (month)	48.7±7.1	31.0±9.0	>0.05
Weight (kg)	13.6±1.3	9.4±1.9	>0.05
MPAP (mmHg)	42±2.1	32.3±9.3	>0.05
LVEF (%)	70.6±0.8	69.0±1.9	>0.05
Rvedd (mm)	28.3±1.3	27.0±3.8	>0.05
Lvedd (mm)	31.6±1.2	30.6±3.8	>0.05
Qp/Qs	2.5±0.2	2.6±0.7	>0.05
Gradient (mmHg)	37.5±9.2	50.7±4.6	**<0.05**
CPB (min)	155.7±18	107±5.4	**<0.05**
ACC (min)	110±13	81.6±5	**0.054**
cTNI (ng/lt)	47.3±2.7	27.4±2.9	**<0.01**
Lactate (mmol/lt)	15.3±8.3	4±0.5	**<0.01**

SE: Standard error; MPAP: Mean pulmonary arterial pressure; LVEF: Left ventricular ejection fraction, Rvedd: Right ventricular end-diastolic diameter, Lvedd: Left ventricular end-diastolic diameter; Qp/Qs: Ratio of pulmonary blood flow (Qp) to systemic blood flow (Qs); CPB: Cardiopulmonary bypass time; ACC: Aortic cross clamp time; cTNI: Cardiac troponin I.

32.2±9.2 mmHg in the non-mortality group (p>0.05). The mean LVEF value (%), RVEDD and LVEDD, and gradient on VSD were found to be similar between the groups (Table 1).

When the operation data were analyzed, CPB time and cross-clamp time were different between the two groups. Although cross-clamp time was longer in the mortality group, it was not statistically significant (110.17±13.07 min vs. 81.52±5.05 min; p=0.054). CPB time was longer in the group with mortality (155.7±18.2 min vs. 107.0±5.4 min, p<0.05). cTNI levels (mortality group 47.3±2.7 ng/l; non-mortality 27.4±2.9 ng/l; p<0.05) and lactate levels (mortality group 15.3±8.3 mmol/lt vs. non-mortality 4.1±0.5 mmol/lt; p<0.01) were significantly different between the two groups (Table 1).

Analysis of Data According to the Increase in the cTNI Value

The cohort was also divided into 2 groups according to the study, with the cut-off point of cTNI at 35 ng/mL.[8] It was found that an increase in cTNI value over 35 ng/lt was associated with the patient's weight, CPB duration time, and LVEDD values (p<0.05). The effect of other pre-operative parameters was not statistically significant (Table 2). Mortality was seen in 4 patients in the higher cTNI group; this was statistically significant (p<0.01).

Analysis of Data According to the Serum Lactate Values

The cut-off value for serum lactate was 3,5 mmol/lt. No relationship was found between the pre-operative parameters and the increase in lactate level (p>0.05) (Table 3). Cross-clamp time was longer in the high lactate group (lactate >3.5 mmol/lt: 94.6±9.2 min vs. lactate <3.5 mmol/lt: 76.7±3.9 min (p<0.05)) (Table 3).

Discussion

LCOS, defined as low tissue perfusion combined with low systemic blood pressure as a result of myocardial dysfunction, generally occurs 6–18 h after the operation and has an important cause-and-effect relationship among major adverse cardiac events.[9]

The main reasons for LCOS after CHS are multifactorial and associated with the inflammatory effects of prolonged CPB time and myocardial ischemia related to aortic cross-clamp time.

Monitoring lactate and cTNI values to detect early phases of LCOS has been investigated in many different studies with heterogeneous patient groups. In our study, we wanted to investigate how effectively these biomarkers were related to mortality.

In a study of 460 patients who underwent surgery for complex congenital heart disease, associated mortality was reported in 7 of 16 patients who developed MOD after LCOS.[6]

In our mortality group, three of our patients developed severe right ventricular failure after surgery and lost in 48 h after surgery. We noticed that LCOS and then MOD were responsible for the mortality of these patients.

There was an increase in hospital mortality when the serum lactate levels were above 4.8 mmol/L. The same study emphasized that age, CPB duration, cross-clamp duration, and intraoperative lowest hematocrit value are effective in increasing post-operative lactate levels.[10] Munoz et al. stated that changes in serum lactate levels higher than 3 mmol/l during CPB showed high sensitivity (82%) and specificity (80%) for mortality.[11,12] In our study, serum lactate levels were higher in the mortality group, and the difference was statistically significant (p<0.05).

Table 2. Analysis of data according to cTNI value

Variable	cTnI <35 ng/mL	cTnI >35 ng/mL	p
Age (month)	53.2±0.5	20.4±4.4	0.32
Weight (kg)	15.8±2.5	9.6±0.7	**0.02**
Qp/Qs	2.4±0.3	2.6±0.1	0.603
Mpap (mmhg)	27.8±2.4	36.1 ±3.3	**0.06**
LVEF (%)	69.9±1.1	71.7±1.0	0.241
Lvedd (mm)	34.2±1.6	27.9 ±1.2	**0.04**
CPB	99±7.1	123.7±8.2	**0.03**
ACC	80.8±8.9	88.5±29.3	0.47
ICU (day)	1.8±0.3	3.2±1.6	**0.062**
Mortality (n)	n=1	n=5	<0.01

Table 3. Analysis of data according to the serum lactate values

Variable	Lactate <3.5 mmol/lt Mean±SE	Lactate >3.5 mmol/lt Mean±SE	p
Age (month)	45.4±9.0	48.1±9.2	0.82
Weight (kg)	12.1±1.2	14.4±2.3	0.372
Mpap (mmHg)	34.3±2.7	29.5±3.2	0.26
LVEF %	70.5±0.9	70.2±1.0	0.84
Lvedd (mm)	30.9±1.7	32.1±1.3	0.62
Rvedd (mm)	28.4±1.7	27.8±1.5	0.804
Gradient (mmhg)	50.1±6.2	48.3±5.8	0.835
CPB (min)	107.8±6.1	118.2±9.7	0.358
ACC (min)	76.7±3.9	94.6±9.2	0.045
cTnI (ng/lt)	25.2±3.5	35.5±3.7	0.056

In a prospective study conducted in patients who underwent pediatric cardiac surgery under the age of 18 months, it was shown that a cross-clamp time of more than 90 min or a lactate value of more than 2.4 mmol/L in the first 4 h of the post-operative period were alone predictive of the occurrence of post-operative LCOS.[8]

Many studies suggest that prolonged CPB duration, operation weight, and age are associated with increased lactate levels. In our study, we found that aortic cross-clamp time was the only related factor.

The cTNI value measured in patients in intensive care on the first post-operative day has also emerged as a special indicator of myocardial ischemia and has been demonstrated in many studies.[4,7,13,14] A higher than 35 ng/mL cTNI value at the 4th post-operative hour was defined as an independent risk factor for mortality.[14–16] Routine monitoring of cTNI with prolonged cross-clamp time allows early diagnosis of the development of LCOS in the post-operative period. cTNI value >13 ng/mL at the 4th post-operative hour shows 78% sensitivity and 72% specificity in the early diagnosis of LCOS development.[14] Increased cTNI values are related to an increased need for inotropes, a prolongation of extubation time, and a longer stay in the ICU.[14] Immer et al.[17] measured the cTNI values at the 4th post-operative hour in 73 patients who underwent pediatric cardiac surgery and found that the highest values (above 35 ng/mL) were reached in the first 24 h. In our cohort, higher cTNI (above 35 ng/mL) was associated with prolonged CPB duration, lower patient weight, and elevated MPAP.

Myocardial protection techniques during surgery become even more important, especially in patients affected by pulmonary hypertension caused by VSD. Although standardization has been achieved in cardioplegia techniques, the weight (kg) of the patients is generally taken into account in these techniques. Pre-operative awareness of ventricular hypertrophy, in the amount and types of cardioplegia to be given, will help provide effective myocardial protection.

Also, milrinone infusion has been found to have a prophylactic effect and reduce mortality in pediatric complex open heart surgery cases.[16] If there is no response, extracorporeal circulatory support may be considered in the early period.[17]

Study Limitations

Our study has limitations. The present study is limited by its retrospective nature and single center. The number of cases is limited.

Conclusion

Serum lactate levels should be monitored closely in the first 24 h after pediatric cardiac surgery. In the biochemical follow-up of these patients after surgery, it should be kept in mind that elevated serum lactate and cTNI may be predictors of mortality. Simultaneous elevation of cTNI values should suggest early supportive treatments to reduce mortality.

Disclosures

Ethics Committee Approval: The study was approved by the Türkiye Higher Specialization Training and Research Hospital Ethics Committee (no: 300, date: 01/02/2013).

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