Relation Between Cerebral Perfusion Changes and Mortality Scores During Cardiopulmonary Bypass at Adult Cardiac Surgery

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ABSTRACT

Introduction: This study aims to investigate the correlation between cerebral perfusion changes and mortality rate in individuals undergoing adult cardiac surgery.

Patients and Methods: Between April 2018-August 2018, 91 adult individuals who underwent open heart surgery with cardiopulmonary bypass (CPB) were prospectively evaluated. Cerebral perfusion was monitored via near-infrared spectroscopy (NIRS). The NIRS values were recorded at four intervals: T0, just before CPB; T1, cooling period (time taken to reach targeted hypothermia); T2, warming period (time taken to reach normal body temperature); and T3, following minutes of termination of CPB. Euro Score II and Acute Physiology and Chronic Health Evaluation (APACHE) II scores were recorded for each individual.

Results: The operations performed include coronary artery bypass surgery (n= 41, 45%), valvular surgery (n= 47, 51%), and coronary artery bypass combined with valvular surgery (n= 3, 4%). Median Euro Score II was calculated to be 1.1 (range 0.7-36.6), and median APACHE II score was calculated to be 6 (range 0-23). Mortality occurred in four individuals for whom the Euro Score II C index was 0.702 (confidence interval, 0.411-0.993; p= 0.048) and APACHE-II score C index was 0.871 (confidence interval, 0.660-1; p= 0.010). During the operative period, cerebral NIRS values decreased during T3 period, and significant changes occurred at T0-T3 period, consequently leading to an increase in the APACHE-II scores and the prediction of mortality.

Conclusion: The changes at NIRS values were related with higher mortality, morbidity, and predicting scores. It is now suggested that these changes can eventually be a good guide and predictor for the management of patients during preoperative and postoperative periods.

Key Words: Adult cardiac surgery; cardiopulmonary bypass; cerebral NIRS

Erişkin Kalp Cerrahisinde Kardiyopulmoner Baypas Sırasındaki Beyin Perfüzyonu ile Mortalite Skorlarının Etkileşimi

ÖZET

Giriş: Bu çalışmada erişkin kalp cerrahisi ameliyatları sırasındaki beyin perfüzyonu ile mortalite skorlarının etkileşimlerinin araştırılması amaçlandı.

Hastalar ve Yöntem: Nisan 2018-Ağustos 2018 tarihleri arasında kliniğimizde kardiyopulmoner baypas (KPB) ile ameliyat edilecek erişkin hastalar çalışmaya dahil edildi (n= 91). Beyin perfüzyonunu belirlemek için "Near Infrared Spectroscopy (NIRS)" yöntemi kullanıldı. Ölçümler dört zaman aralığında yapıldı. T0: KPB öncesi, T1: soğuma periyodu, T2: ısınma periyodu, T3: KPB sonrası. Mortalite skorları olarak EuroSCORE II ve "Acute Physiology and Chronic Health Evaluation (APACHE)" II skoru değerleri her bir hasta için kaydedildi.

Bulgular: Ameliyat verileri, koroner arter baypas cerrahisi (n= 41, %45), kapak ameliyatları (n= 47, %51), koroner arter baypas cerrahisi ve kapak ameliyatlarının birlikte uygulandığı hastalar (n= 3, %4) olarak saptandı. Ortalama Euroscore II 1.1 (0.7-36.6) ve ortalama APACHE II skoru 6 (0-23) bulundu. Ölüm gelişen dört hastada EuroSCORE II C indeksi 0.702 (Confidence interval 0.411-0.993, p= 0.048) ve APACHE II score C indeksi 0.871 (Confidence interval 0.660-1, p= 0.010) belirlendi. Ameliyat sırasında T3 dönemindeki NIRS ölçüm değerleri düşük bulunan ve T0-T3 periyodundaki NIRS değeri değişiklikleri anlamlı olan hastalarda APACHE II skoru ölçümlerinde anlamlı değişiklik saptandı.

Sonuç: NIRS ölçümlerindeki değişiklikler, mortalite ve morbidite skorlama yöntemleri ölçümleriyle paralellik gösterir. Bu nedenle ameliyat öncesi ve sonrası dönemdeki hasta yönetimi açısından NIRS ölçümü iyi bir belirteçtir.

Anahtar Kelimeler: Erişkin kalp cerrahisi; kardiyopulmoner baypas; serebral NIRS

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INTRODUCTION

Hemodynamic monitoring is a routine procedure for cardiac surgery; however, microcirculatory changes cannot be detected only using standard monitoring methods(1). Near-infrared spectroscopy (NIRS) is a noninvasive procedure used to monitor regional oxygenation in cerebral or somatic tissues, measuring oxygen saturation of hemoglobin in venous capillaries, which quantitatively provides the greatest contribution to the vascular bed(2). NIRS has been documented to predict acute and chronic neurocognitive disorders. It is also documented that NIRS has proven its usefulness for kidney and other somatic areas(3,4).

Scoring methods to evaluate the operative and intensive care unit (ICU) mortality risks, such as The European System for Cardiac Operative Risk Evaluation Score (Euro Score II) and Acute Physiology and Chronic Health Evaluation (APACHE) II, have been previously created(5,6). These scoring methods are advantageous for the standardization of operative risk rating and calculation, guiding clinical decisions and forming an objective database(7).

There is still limited knowledge about how NIRS changes may affect the mortality scoring systems in terms of cerebral oximetry values. In this study, we aim to correlate the probable relation between NIRS value changes, Euro Score II and APACHE-II scores, and mortality/morbidity rates.

PATIENTS and METHODS

Between April 2018-August 2018, 91 adult individuals who underwent open heart surgery with cardiopulmonary bypass (CPB) were prospectively evaluated. This study was approved by the Institutional Ethics Committee (ethical approval number: 03.10.2018/3-2) and conducted in accordance with the principles of the Declaration of Helsinki. Patients who underwent adult congenital cardiac surgery, redo cardiac surgery, and emergent operations and individuals with a comorbidity of significant carotid artery stenosis were excluded from the study.

Intraoperative Anesthesia Management

The patients were premedicated 30 minutes prior to anesthesia induction by intravenous administration of 0.03 mg/kg midazolam. Then, electrocardiography, pulse oximetry, and invasive blood pressure monitoring via the radial artery were performed. Anesthesia induction was performed using intravenously (IV) applied midazolam 0.1-0.2 mg/kg, IV fentanyl 1.0-1.5 μg/kg, propofol 2 mg/kg, and IV rocuronium 0.6 mg/kg. Continuous infusion of fentanyl 0.3 μg/kg/h and sevoflurane (concentrations from 0.5% to 3%) was used for maintenance of hypnosis. Ventilator settings were adapted to maintain normocapnia. Dexamethasone at a dose of 1 mg/kg was administered to all patients. Subsequent to anesthesia induction and intubation, an internal jugular vein catheter was inserted into all patients. Body temperature was monitored using thermal sensors placed in the nasopharynx or rectum.

Cardiopulmonary Bypass

Following systemic heparinization, arterial and venous cannulas were placed, and consequently, CPB was traditionally led with a pump flow rate of 2.4 L/min/m^2 of body surface area (BSA) calculated on measured patient weight and height. BSA was calculated using the Mosteller formula $\{[(\text{height} \times \text{weight})/3600]\}^{1/2}$. The body temperature was reduced to 32°C. No patient underwent hypothermic circulatory arrest.

The ascending aorta was cross-clamped, and cardiac arrest was then achieved by antegrade isothermic blood cardioplegia. A roller pump with membrane oxygenator was used, and standard pump flow rate was regulated according to cardiac index and body temperature to maintain a mean arterial pressure of 50-70 mmHg. Proportional with BSA, pump prime solution comprised Isolyte, bicarbonate, methylprednisolone, heparin, gelofusine, and mannitol. To preserve the myocardium, blood cardioplegia was performed in 15- to 20-minute intervals during cross-clamping. Subsequent to cross-clamping, topical cooling was employed in all patients. Alpha-stat arterial gas monitoring and activated clotting time monitoring were performed during CPB. Subsequent to the completion of surgical repair, upon confirmation that body temperature was normothermic and hemodynamic variables were stable, CPB was terminated.

NIRS Monitoring

A four-channel trend monitor (Somanetics 5100B, Troy, MI, USA) was used for cerebral monitoring. The NIRS sensor was placed on the mid-forehead following endotracheal intubation. The values measured during post-induction were marked as baseline, and changes were recorded. The NIRS values were recorded at four intervals: T0, just before CPB; T1, cooling period (time taken to reache targeted hypothermia); T2, warming period (time taken to reach normal body temperature); and T3, following minutes of termination of CPB. The NIRS changes between these intervals were also evaluated.

Euro Score II

Risk scoring system is important for operative risk analysis, planning the surgical procedure, and informing the patient about the risks of the operation. Standard Euro Score was formed initially in 1999, updated in 2003 as logistic Euro Score, and finally re-updated in 2011 as Euro Score II. Preoperative surgical risk scoring was measured according to Euro Score II system, and the operative risk was determined for every patient. The patients were grouped as follows: low risk group (score 0-2), moderate risk group (score 3-5), and high-risk group (score > 5)(5,8).

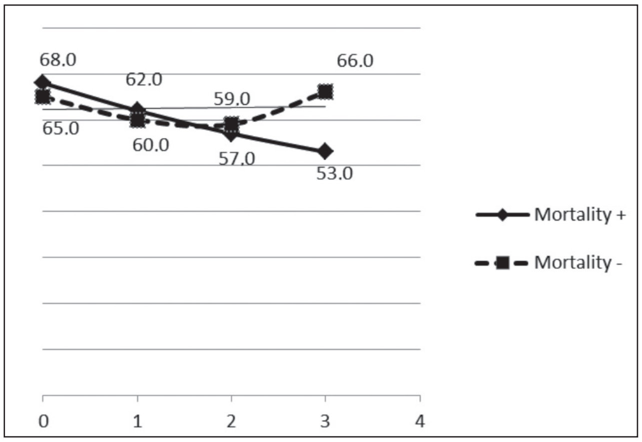

Figure 1. The effect of mortality on cerebral NIRS changes in different periods of cardiopulmonary bypass.

T0, p= 0.556; T1, p= 0.930; T2, p= 0.730; T3, p= 0.036.

APACHE-II

The APACHE-II scoring system comprises parameters, including body temperature, mean artery pressure, heart rate, ventilation rate, PaO_2 rate, arterial pH value, serum bicarbonate levels, serum sodium levels, serum potassium levels, serum creatinine levels, hematocrit, white blood cells, Glasgow Coma Score, and age. These parameters were used to predict the mortality rate[(6)]. Death, which occurs at preoperative or postoperative 30 days, was described as mortality.

Statistical Analysis

Statistical analysis was performed using SPSS for Windows version 21.0 (SPSS Inc., Chicago, IL, USA).Normally distributed continuous variables were expressed in means ± standard deviation, whereas categorical variables were expressed in numbers and percentages. Demographic features and perioperative variables were compared using the Mann-Whitney U and chi-square tests. The NIRS values recorded at four time points during the operation were then compared using the Mann-Whitney U test for both all patients and individually for each group.

The analysis of the discriminatory ability of the surgical risk stratification methods was performed using the C statistic comparison with the calculation of both receiver operating characteristic (ROC) curves of the two methods and area under curve (AUC). We defined the cut-off as closest point to sensitivity = specificity = 1.0 on ROC curve. An AUC of 0.90-1.0 indicated excellent; 0.80-0.89, very good; 0.70-0.79, acceptable; and < 0.70, nonsignificant indicated no usefull value. A p value of < 0.05 was considered statistically significant.

RESULTS

This study comprised 91 individuals [60 (65.9%) men and 31 (34.1%) women] whose mean age was 54 ± 14 years (range 17-84) and median BSA was 1.88 m^2 (range 1.36-2.28). The operations performed included coronary artery bypass surgery (n= 41, 45%), valvular surgery (n= 47, 51%), and coronary artery bypass combined with valvular surgery (n= 3, 4%). Median Euro Score II was calculated to be 1.1 (range 0.7-36.6), whereas median APACHE-II score was calculated to be 6 (range 0-23). Demographic data and operative details were listed in Table 1. Mean CPB and cross-clamp times were 91 ± 37 and 55 ± 34 minutes, respectively.

Mortality occurred in four cases (4.3%). The reasons for mortality were low cardiac out-put syndrome in three patients, whereas vasoplegia syndrome in the fourth patient. NIRS values measured at the T3 interval were significantly related to higher mortality (p= 0.036) (Figure 1).

AUC of T0-T3 NIRS changes was 0.934 (confidence interval, 0.839-1; p= 0.003), T1-T3 NIRS change was 0.805 (confidence interval, 0.572-1; p= 0.040), and T2-T3 NIRS change was 0.810 (confidence interval, 0.487-1; p= 0.038); all of these changes were considered significant for mortality in CPB period.

The effect of NIRS changes on mortality is presented in Table 2. According to these results, a decrease in NIRS value at T0-T3 intervals > 10% was related to significantly higher mortality (p< 0.05).

The relation between mortality and Euro Score II C index was 0.702 (confidence interval, 0.411-0.993; p= 0.048) and APACHE-II score C index was 0.871 (confidence interval, 0.660-1; p= 0.010). These results were significant for predicting the risk of mortality.

Table 1. Patient characteristics

Patient characteristics	n= 91
Sex (male/female)	60/31
Median age, years (range)	56 (17-84)
Median body surface area, m^2 (range)	1.88 (1.36-2.28)
Echocardiographic variables	
LV ejection fraction, median (range)	55 (40-75)
Ejection fraction < 55%, n (%)	10 (11)
Operative details, n (%)	
CABG	41 (45)
CABG + Mitral valve surgery	3 (3.3)
Mitral valvesurgery	25 (27.4)
Mitral + Tricuspid valve surgery	12 (13.1)
Aortic valvesurgery	10 (10.9)
Mortality (yes/no)	4/87
Euroscore total median (range)	1.1 (0.7-75.1)
Mortality* median (range)	2.7 (0.7-75.1)
No mortality* median (range)	1.2 (0.7-16.1)

*p= 0.001.

LV: Left ventricle, CABG: Coronary artery bypass grafting.

Table 2. Relationship between mortality and NIRS changes during CPB

NIRS changes	T0-T1	p	T0-T2	p	T0-T3	p	T1-T2	p	T1-T3	p	T2-T3	p
NIRS 10%; Mortality, n (%)	2 (50)	0.991	3 (75)	0.323	3 (75)	**0.038**	2 (50)	0.191	2 (50)	0.058	3 (75)	**0.001**
NIRS 15%; Mortality, n (%)	2 (50)	0.264	2 (50)	0.310	3 (75)	**0.004**	2 (50)	**0.048**	2 (50)	**0.014**	1 (25)	**0.044**
NIRS 20%; Mortality, n (%)	-(0)	0.991	2 (50)	0.125	2 (50)	**0.002**	1 (25)	0.205	2 (50)	**0.004**	-(0)	0.991

NIRS: Near-infrared spectroscopy, CBP: Cardiopulmonary bypass, T0: Base NIRS record (before CPB), T1: NIRS values before cross-clamping, T2: NIRS values after cross-clamping, T3: NIRS values after CPB.

Table 3. Relationship between Euroscore and NIRS changes during CPB

NIRS changes Euroscore median (range)	T0-T1	p	T0-T2	p	T0-T3	p	T1-T2	p	T1-T3	p	T2-T3	p
NIRS change 10% +	1.1 (0.7-75.1)	NS	1.1 (0.7-75.1)	NS	1.2 (0.7-75.1)	NS	1.4 (0.7-75.1)	NS	1.3 (0.7-75.1)	NS	1.3 (0.7-75.1)	NS
-	1 (0.7-4.3)		1 (0.7-8.6)		1 (0.7-16.7)		1 (0.7-14)		1 (0.7-14)		1 (0.7-14)	
NIRS change 15% +	1 (0.7-4.3)	NS	1 (0.7-75.1)	NS	3.1 (0.7-75.1)	**0.010**	1.2 (0.7-75.1)	NS	1.2 (0.7-75.1)	NS	1.2 (0.7-75.1)	NS
-	0.9 (0.7-75.1)		1.1 (0.7-16)		1.1 (0.7-16.7)		1 (0.7-16.7)		1.1 (0.7-16.7)		1.1 (0.7-16.7)	
NIRS change 20% +	1 (0.7-3.9)	NS	1.2 (0.7-75.1)	NS	1.1 (0.7-16.1)	**0.002**	1.2 (0.7-75.1)	NS	1.1 (0.7-75.1)	NS	-	NS
-	0.9 (0.7-75.1)		1 (0.7-16)		38.1 (0.7-75)		1 (0.7-16.7)		1.1 (0.7-16.7)		1.1 (0.7-75)	

CBP: Cardiopulmonary bypass, NIRS: Near-infrared spectroscopy.

Table 4. Relationship between APACHE-II score and NIRS changes during CPB

NIRS changes APACHE II median (range)	T0-T1	p	T0-T2	p	T0-T3	p	T1-T2	p	T1-T3	p	T2-T3	p
NIRS change 10% +	6 (1-12)	NS	7 (0-23)	NS	10 (2-23)	**0.040**	8 (1-20)	NS	8.5 (2-23)	NS	20 (6-23)	**0.022**
-	6 (0-23)		6 (1-11)		6 (0-10)		6 (0-23)		6 (0-13)		6 (0-13)	
NIRS change 15% +	6 (1-12)	NS	6 (0-23)	NS	11 (2-23)	**0.025**	7 (1-20)	NS	10 (2-23)	NS	-	NS
-	6 (0-23)		6 (1-11)		6 (0-10)		6 (0-23)		6 (0-13)		6 (0-23)	
NIRS change 20% +	6 (1-11)	NS	6 (0-23)	NS	21 (20-23)	**0.003**	5 (1-23)	NS	20 (2-23)	**0.035**	-	NS
-	6 (0-23)		6 (1-12)		6 (0-12)		6 (0-20)		6 (0-13)		6 (0-23)	

CBP: Cardiopulmonary bypass, NIRS: Near-infrared spectroscopy.

The relation between NIRS percentages and Euro Score II is presented in Table 3. Euro Score II was calculated to be significantly higher in cases of NIRS change > 15%.

The effect of NIRS percentages on APACHE-II scoring system is presented in Table 4. A decrease in NIRS value at T0-T3 interval > 10% was significantly related to APACHE-II scoring system ($p< 0.05$).

DISCUSSION

In routine cardiac operations during CPB, blood circulation is dependent on various factors, including, but not limited to, artery pressure, temperature changes, and some other conditions; however, blood pressure alone may not be a proper indicator of systemic perfusion. NIRS provides continuous real-time monitoring of cerebral perfusion where microcirculation is also detected even during CPB circulation[9]. As a main finding of our study, we noticed that cerebral NIRS value changes (10%, 15%, and 20% decrease) were correlated with higher mortality and APACHE-II scores.

The normal cardiac index is 2.4L/m^2/min, and this weight-based protocol provides enough flow rate during CPB. In a study by Mittnacht, et al., it was reported that NIRS is a reliable indicator of tissue perfusion[10]. If NIRS values decrease, pump flow rate would be increased; either it had been at a low flow rate or normal flow rate to provide adequate perfusion.

Murkin, et al. have reported that NIRS monitoring is capable of diagnosing silent ischemia of the brain, and consequently, ischemia-related complications can be avoided[9]. The relation between NIRS value decrease of > 25% and cerebral ischemia has also been previously confirmed[11]. Furthermore, 50 pediatric cardiac cases have been evaluated, and it is documented that NIRS values, CPB flow rate, blood pressure, and serum lactate levels revealed correlation with each other. The effectiveness of NIRS for brain tissue protection has been concluded, and routine usage of NIRS has been proposed[12]. In contrast, Erdoes had conducted a study with eight patients and reported that NIRS had limited utility for monitoring focal cerebral ischemia[13].

NIRS monitoring is a real-time hemodynamic follow-up instrument. This aspect of NIRS has been supported by a study performed within pediatric patients who had undergone cardiac catheterization. Significant NIRS value decreases have been related with arrhythmia, hypoxic spells, and similar complications. Furthermore, a decrease in NIRS value is an important early warning for the clinician[14,15]. Data about the relation between NIRS changes and mortality is limited[16]. In our study, the relation between mortality and NIRS decrease > 10% at T0-T3 period, which is the time of CPB termination, was evaluated to be statistically significant. In addition, as the rate of NIRS change increases, its relation with mortality becomes more significant. Probable reasons of this result might include hypovolemia, hypothermia, low cardiac out-put, and anemia. In case of a significant decrease in NIRS values during the aforementioned periods, problem-related solutions might be performed to avoid higher mortality risk, stabilize the patient's hemodynamic status, and eliminate major signs of hemodynamic deterioration.

It was reported that the use of NIRS during CPB at cardiac surgery did not result in reduction of mortality and injuries of the brain, heart, or kidneys[9,17-20]. NIRS changes during CPB have not been related to neurocognitive dysfunctions[17]. Despite the literature demonstrating no clinical benefits of NIRS-based algorithms during CPB, our study reports that NIRS-correlated predicting scores, such as APACHE and Euro Score II, are helpful in avoiding mortality and morbidity. In the reported study, the quality of evidence was either low or very low for all of the measured outcomes.

In adult cardiac surgeries, it is well studied that higher Euro Score II scores are related with higher mortality rates. Various studies have shown that Euro Score II is a successful scoring system for predicting mortality[5-8]. In our study, mortality rate was higher in patients with high Euro Score II rates, as expected. Statistical analyses with ROC interval showed that Euro Score II scoring is successful for predicting mortality. Furthermore, we detected a relation between NIRS value changes during CPB and Euro Score II scoring; high Euro Score II rates were correlated with a decrease in NIRS values of > 15%. This finding is confirmatory that NIRS value changes could be considered as a safe and effective predictor of mortality as well as preoperatively calculated Euro Score II score.

CPB causes a wide range of hemodynamic, inflammatory, and immunological effects because of arterial blood flow, body temperature changes, and extracorporeal circuits; therefore, leucocytes, thrombocytes, complement systems, and coagulation cascades are activated[21,22]. This chain reaction results in tissue perfusion defects, which eventually causes an increase in the mortality predicting score (APACHE-II) in an ICU setting. A previous study showed that APACHE-II scoring system is effective for predicting the mortality at an early period[23]. Furthermore, a study consisting of 523 cases, which was performed to detect ICU mortality, reported the usefulness of APACHE-II scoring system[24]. In our study, cerebral NIRS value changes during CPB were related to higher APACHE-II scores for patients undergoing adult cardiac surgery. This result became an alerting sign for us to make maneuvers for increasing tissue perfusion during and after CPB and in the ICU department. Statistical analyses with ROC interval showed that APACHE-II scoring is successful for predicting mortality.

The major limitation of our study is the single-center nature of the data available for analysis. The other limitation is heterogeneous character of the study because coronary artery and valvular operations were evaluated together.

CONCLUSION

In the present study, NIRS value changes during CPB in adult cardiac surgery were found to be related with higher Euro Score II and APACHE-II scores, which are powerful predictors of mortality and morbidity. Consequently, we propose NIRS monitoring as a standard procedure in cardiac operations to possibly reduce mortality and morbidity via intraoperative maneuvers to maintain optimal microcirculation.

CONFLICT of INTEREST

The authors reported no conflict of interest related to this article.

AUTHORSHIP CONTRIBUTIONS

Concept/Design: All of authors.
Analysis/Interpretation: All of authors.
Data Acquisition: All of authors.
Writting: All of authors.
Critical Revision: All of authors.
Final Approval: All of authors.

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