Evaluation of VEP parameters in patients before and after cardiopulmonary by-pass surgery

Alper Güneş · Şerife Gülhan Konuk · Helin Deniz Demir · Semiha Kurt · Erdinç Naseri · Ünal Erkorkmaz

Methods Thirty-one patients were included in the study. After a full ophthalmological evaluation, PVEP was assessed in the pre and postoperative periods. Operative times, hematological parameters, blood pressures, number of transfusions, body temperatures, anaesthetic drugs and systemic illnesses were recorded for each patient.

Results The mean age of the patients were 59 ± 10.4 years. There was 22 men and 9 women in the study. Only 3 of them needed transfusion during the surgery. The mean duration of the surgery was 3.2 ± 0.7 h. None of the patients had a history of visual disturbance or postoperative ischemic optic neuropathy. The mean VEP P100 amplitude was not statistically significantly different but the mean VEP P100 latency showed statistically significant difference between the preoperative and postoperative periods. \(p = 0.014\) This significance was more apparent in patients with systemic illnesses. \(p = 0.023\) There was a positive correlation between the age and VEP P100 latency \(r = 0.402, p < 0.05\).

Conclusions Although surgical techniques and equipments are developing each day in the field of cardiopulmonary bypass surgery, the contributing factors such as hypothermia, anemia and diabetes still seem to affect neurophysiological functions even after a noncomplicated surgery.

Keywords Cardiopulmonary by-pass surgery · VEP P100 latency · Systemic illnesses · Aging · Anemia · Hypothermia
**Introduction**

Extracorporeal circulation (ECC) during cardiopulmonary by-pass surgery (CPBS), may cause ischemia and infarction by hypoperfusion and microembolus formation. It affects whole body but especially the perfusion sensitive organs brain and eye. Arterial system of the eye is an end-arterial system and the retinal and optic nerve vessels regulate the perfusion pressure changes by myogenic and metabolic processes instead of autonomic system.

Cerebrovascular accident findings related to the involved area as a result of embolism and hypoperfusion of the brain, anterior and/or posterior ischemic optic neuropathy, retinal hemorrhages, soft exudates, angiographic and postmortem shown ischemic areas of chorioretinal circulation, visual field defects and permanent or temporary visual acuity loss has been reported [1, 2].

CPBS related ischemic optic neuropathy (ION) has a devastating course and visual deterioration is usually severe and persistent. Alterations in visual evoked potentials (VEP) after ION have been well established and it is known that pattern VEP (PVEP) amplitude decreases after acute ION. There are also reports about the elongation of PVEP latency in acute ION [3]. VEP is used to assess the functional disturbances from retina to visual cortex and intraoperative measurement of VEP has been reported to be useful in monitoring neurophysiological functions as well [4–6].

In this study, we aimed to evaluate the optic nerve involvement and the impact of contributing factors in patients with CPBS by assessing the PVEP in the pre and postoperative periods.

**Methods**

Thirty-one patients were included in the study. Patients with glaucoma, arteritic or nonarteritic ischemic optic neuropathy, multiple sclerosis, alcohol and tobacco consumption, nonproliferative and proliferative diabetic retinopathy were excluded from the study. Cases with complicated surgery such as intraoperative excessive bleeding, prolonged anesthesia and/or postoperative cardiac resustation were all excluded from the study as it will affect brain functions and VEP p100 latency consequently.

After a full ophthalmological evaluation, PVEP was assessed before and after the surgery. Duration of surgery, hematological parameters, blood pressures, number of the transfusions, body temperatures, anaesthetic drugs and systemic illnesses were recorded for each patient.

This study was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. Written informed consent from all participants and institutional ethics committee approval was obtained.

PVEP was recorded within 10 days before and between the 7th and 10th days after the surgery when the patients were healthy enough for VEP assessment. Data were obtained during the routine hospitalization of cardiovascular surgery 10 days prior to surgical preparation. A period close to the date of operation was chosen to exclude other effects in the perioperative period.

During VEP recordings, all patients were seated comfortably in a semidarkened room, and exposed to the stimuli coming from a television monitor 1 m away from the tested eye. Vision was central and monocular. Patients were asked to keep their eye on the central fixation point and warned verbally whenever the fixation was lost or not. Recordings were performed using Medelec Synergy EMG machine. A total analyze time of 500 ms, in other words a sweep speed of 50 ms/division for each store. Stimulation rate was 1.9 pps. Single stimulation was used. VEP check sizes were 8 and 16. Amplifier range was 2.5 mV. Acquisition duration was 300 ms. The mean luminance was 43.3 cd/m² and the the contrast was 100%. Low and high frequency filter settings were predetermined at 1.0 Hz, and 100 Hz, respectively. The international 10–20 system was used to insert electrodes. VEPs were recorded from 5 channels (T5-Cz, O1-Cz, Oz-Cz, O2-Cz, and T6-Cz). The ground electrode was attached on the forearm. Recordings were obtained by monocular checkerboard pattern reversal stimulation. An average of 200 runs were taken, and each run was checked for reproducibility by a second waveform stored in the memory system. For each eye, the first prominent positive (downward deflection) peak P100 was obtained. The latencies to the peak P100 and peak-to-peak amplitude of P100 in pre/postoperative periods were assesed by software and then controlled by a blinded researcher.
Kolmogorov–Smirnov test was used to evaluate the normality of the distribution of variables. Accordingly, it was seen that all variables displayed a normal distribution ($p > 0.05$ for all variables). Therefore, Independent samples $t$ test was used to compare the VEP P100 latency values, between independent groups. Paired sample $t$-test was used to compare continuous variables between pre and postoperative periods. Pearson correlation coefficient was performed to assess correlations among variables. Continuous variables were presented as the mean ± standard deviation, and categorical variables as numbers. A $p$-value < 0.05 was considered significant. Analyses were performed using a commercial software package (IBM SPSS Statistics 19, SPSS inc., an IBM Co., Somers, NY).

### Results

Mean age of the patients were $59 \pm 10.4$ years. There were 22 men and 9 women in the study. Eight subjects did not have a systemic disease. Only 3 of them needed transfusion during the surgery. The details of the parameters evaluated were shown in Table 1.

None of the patients had a history of visual disturbance or postoperative ION. Each patient anesthetized according to the principles of standardized anesthesia in these patients. The mean VEP P100 amplitude was not statistically significantly different but the mean VEP P100 latency showed statistically significant difference between the preoperative and postoperative periods. ($p = 0.014$) (Table 2).

### Table 1  Demographic characteristics of the study patients

| Characteristics                  | Data were shown as mean ± standard deviation and n (%) |
|----------------------------------|--------------------------------------------------------|
| Age (years)                      | 59.03 ± 10.43                                          |
| Gender                           |                                                        |
| Female                           | 9 (29%)                                                |
| Male                             | 22 (71%)                                               |
| Associated Systemic Illness      |                                                        |
| No                               | 8 (25.8%)                                              |
| DM                               | 5 (16.1%)                                              |
| HT                               | 9 (29%)                                                |
| Dyslipidemia                     | 2 (6.5%)                                               |
| CHD                              | 1 (3.2%)                                               |
| DM + HT                          | 4 (12.9%)                                              |
| DM + HT + Dyslipidemia           | 1 (3.2%)                                               |
| HT + CHD                         | 1 (3.2%)                                               |
| DM                               |                                                        |
| No                               | 21 (67.7%)                                             |
| Yes                              | 10 (32.3%)                                             |
| HT                               |                                                        |
| No                               | 16 (51.6%)                                             |
| Yes                              | 15 (48.4%)                                             |
| Dyslipidemia                     |                                                        |
| No                               | 28 (90.3%)                                             |
| Yes                              | 3 (9.7%)                                               |
| Systemic Illness                 |                                                        |
| No                               | 8 (25.8%)                                              |
| Yes                              | 23 (74.2%)                                             |
| Blood Transfusion                |                                                        |
| No                               | 28 (90.3%)                                             |
| Yes                              | 3 (9.7%)                                               |
| Operative time (hour)            | 3.17 ± 0.77                                             |
| Systolic blood pressure (mmHg)   | 126.00 ± 17.00                                          |
| Diastolic blood pressure (mmHg)  | 75.50 ± 10.00                                           |
| Intraoperative Hb (g/dl)         | 8.5 ± 0.8                                               |
| Intraoperative Htc (%)           | 25.6 ± 2.4                                              |
| Postoperative Hb (g/dl)          | 8.2 ± 0.5                                               |
| Postoperative Htc (%)            | 24.6 ± 1.5                                              |
| Intraoperative body temperature (°C) | 27.9 ± 0.7                                      |
This significance was more apparent in patients with systemic illnesses especially with diabetes. \( p = 0.023 \) (Table 3).

There was a positive correlation between the age and VEP P100 latency. \( r = 0.402, p < 0.05 \) (Table 4).

### Discussion

Ischemic optic neuropathy is characterised by acute onset painless visual loss. Crowded disc, diabetes, hypertension and anemia are among the risk factors. Also it may be a devastating complication of CPBS [7]. Hypothermia, hemodilution, microembolus formation and prolonged extracorporeal operativen times as well as the advanced age and vascular impairment are well known risk factors for its development after this major surgery [8].

Evaluation of evoked potentials is a noninvasive method of assessment of neuronal conduction and central nervous system functions [9]. VEP has been used as an effective method in monitoring neurophysiological functions during surgical procedures and it is the gold standard electrophysiological method for evaluating the visual pathways [5, 6].

The postoperative elongation of VEP P100 latency in our patients may be multifactorial. Keenan et al. observed elongation of PVEP latency in patients during CPBS and circulatory arrest and found a negative correlation between the hypotermia and latency [5]. They explained this finding by progressive slowing of axonal conduction and increased synaptic delay. The same findings were also reported and the hypothermia related prolonged latency were found to be independent of anesthetic drugs [10].

Iron deficiency has been shown to affect PVEP latency in the childhood group [9, 11]. Iron (Fe), is the cofactor of the enzyme involved in ATP synthesis. ATP is crucial in maintenance of synaptic and axonal conduction in the central nervous system. It is also essential in the synthesis of the dopamine and myelin synthesis [12].

### Table 2

The mean VEP P100 amplitudes and latencies of patients in pre- and postoperative periods

|        | n  | Preoperative | Postoperative | \( p \) |
|--------|----|--------------|---------------|-------|
| Latency (ms) | 31 | 105.96 ± 6.23 | 108.57 ± 8.19 | 0.014 |
| Amplitude (mv) | 31 | 6.84 ± 3.21 | 7.40 ± 3.45 | 0.164 |

Data were shown as mean ± standard deviation and \( n \) (%)

### Table 3

Comparision of VEP P100 latencies of patients with systemic illnesses and diabetes

|        | Preoperative | Postoperative | \( p^* \) |
|--------|--------------|---------------|-------|
| DM No (\( n = 21 \)) | 106.47 ± 4.94 | 107.90 ± 7.89 | 0.231 |
| Yes (\( n = 10 \)) | 104.88 ± 8.57 | 109.99 ± 9.04 | **0.016** |
| \( p^{**} \) | 0.516 | 0.516 | |
| Systemic Illness No (\( n = 8 \)) | 105.75 ± 6.80 | 108.41 ± 11.82 | 0.323 |
| Yes (\( n = 23 \)) | 106.03 ± 6.18 | 108.63 ± 6.85 | **0.023** |
| \( p^{**} \) | 0.915 | 0.950 | |

Data were shown as mean ± standard deviation and \( n \) (%)

*\( p \) values of comparisons between pre and postoperative periods (Paired-samples \( t \)-test). **: *: \( p \) values of comparisons between NA and A groups (Independent samples \( t \)-test). DM Diabetes Mellitus, NA Not available, A available

### Table 4

The correlations between PVEP parameters and age, blood pressures and operative times

|        | Preop latency | Preop amplitude | Postop latency | Postop amplitude |
|--------|---------------|----------------|---------------|-----------------|
| \( r \) | \( p \) | \( r \) | \( p \) | \( r \) | \( p \) | \( r \) | \( p \) |
| Surgery duration | −0.206 | 0.267 | −0.155 | 0.404 | −0.011 | 0.954 | −0.201 | 0.278 |
| Systolic BP | 0.354 | 0.125 | −0.208 | 0.379 | 0.320 | 0.169 | −0.202 | 0.392 |
| Diastolic BP | 0.213 | 0.367 | −0.272 | 0.246 | 0.206 | 0.383 | −0.288 | 0.219 |
| Age | 0.352 | 0.052 | −0.260 | 0.158 | 0.402* | 0.025 | −0.156 | 0.401 |

*\( r \) correlation coefficient, BP Blood pressure
is an important neurotransmitter in the visual and auditory pathways. Iron deficiency anemia related latency delay has been explained both with hypoxia and the requirement of Fe in these critical biochemical reactions [9, 10]. Hemoglobin decrement up to the 10th postoperative day in CPBS patients has been reported as an outcome of bleeding and liquid shift out of the vascular bed [13]. Also changes in Hb concentrations mentioned were reported as a cause for tissue hypoxemia. The recommended Htc concentration is 25% for extracorporeal circulation and tissue oxygenation, and also blood flow can be successfully maintained by Htc concentrations of 35% [14]. Since, our patients experienced mild anemia and related decreases in Htc concentrations during and after the surgery, anemia may be a contributing factor for latency delay in our patients.

Postoperative ischemic optic neuropathy has been shown to be more frequent in diabetics with Htc concentrations lower than 22%. It has been also emphasized that uncontrolled diabetics demonstrated VEP latency elongation [15, 16]. In our study, the pre- and post operative latencies showed statistically significant difference in patients with systemic illnesses (\( p = 0.023 \)) and especially the patients with diabetics. (\( p = 0.016 \)) (Table 3) Lower Htc concentrations and diabetes-related microvascular complications may contribute to the latency elongation as well.

We found a positive correlation between latency and age. As shown in various investigations optic nerve and cortical conduction velocities decreased with aging [17]. Aging may also be a contributing factor in the latency difference in our study.

None of our patients despite PVEP 100 latency elongation experienced ION. Systemic illness especially diabetes and age seems to be a contributing factor to VEP elongation but well-controlled blood pressures and mild anemic course during surgery might prevent the development of ION in our study group.

The major limitation of our study is the small sample size and short-term follow-up of this patients. New studies with larger participitants and longer follow-up period should be constructed to reveal the VEP parameters changes before and after CPBS and it’s affects for the risk of ION.

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**Declarations**

**Conflict of interest** The authors declare that they have no conflict of interest.

**Consent to publish** All participants agreed to the collection and anonymous publication of the data.

**Ethical approval** All procedures performed in studies involv- ing human participants were in accordance with the ethical standards of the Tokat Gaziosmanpaşa University Faculty of Medicine clinical research ethics committee (20-KAEK-23) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

**Informed consent** Informed consent was obtained from all individual participants included in the study.

**References**

1. Nenekidis I, Pournaras CJ, Tsironi E et al (2012) Vision impairment during cardiac surgery and extracorporeal circulation: current understanding and the need for further investigation. Acta Ophthalmol 90(3):e168–e172. https://doi.org/10.1111/j.1755-3768.2011.02317.x
2. Blauth CI, Smith PL, Arnold JV et al (1990) Influence of oxygenator type on the prevalence and extent of microembolic retinal ischemia during cardiopulmonary bypass. Assessment by digital image analysis. J Thorac Cardiovasc Surg 99(1):61–69
3. Holder GE (2004) Electrophysiological assessment of optic nerve disease. Eye (Lond) 18(11):1133–1143. https://doi.org/10.1038/sj.eye.6701573
4. Mukarтиhal G, Radhakrishnan S, Ramasubba Reddy M et al (2005) Statistical analysis of visual evoked potentials in optic neuritis and ischemic optic neuropathy subjects. Conf Proc IEEE Eng Med Biol Soc 2005:1193–1195. https://doi.org/10.1109/EMBS.2005.1616637
5. Keenan NK, Taylor MJ, Coles JG et al (1987) The use of VEPs for CNS monitoring during continuous cardiopulmonary bypass and circulatory arrest. Electroencephalogr Clin Neurophysiol 68(4):241–246. https://doi.org/10.1016/0168-5597(87)90044-x
6. Sasaki T, Ikaura T, Suzuki K et al (2010) Intraoperative monitoring of visual evoked potential: introduction of a clinically useful method. J Neurosurg 112(2):273–284. https://doi.org/10.3171/2008.9.JNS08451
7. Tidow-Kebritch T, Jay WM (2003) Anterior ischemic optic neuropathy following off-pump cardiac bypass surgery. Semin Ophthalmol 18(4):166–168. https://doi.org/10.1080/08820530390895154
8. Trehowan BA, Gilliland H, Popov AF et al (2011) A case report and brief review of the literature on bilateral retinal infarction following cardiopulmonary bypass for coronary artery bypass grafting. J Cardiothorac Surg 6:154. https://doi.org/10.1186/1749-8090-6-154
9. Algarin C, Peirano P, Garrido M et al (2003) Iron deficiency anemia in infancy: long-lasting effects on auditory
and visual system functioning. Pediatr Res 53(2):217–223. https://doi.org/10.1203/01.PDR.0000047657.23156.55

10. Hetzler BE, Boyes WK, Creason JP et al (1988) Temperature-dependent changes in visual evoked potentials of rats. Electroencephalogr Clin Neurophysiol 70(2):137–154. https://doi.org/10.1016/0013-4694(88)90114-9

11. Monga M, Walia V, Gandhi A et al (2010) Effect of iron deficiency anemia on visual evoked potential of growing children. Brain Dev 32(3):213–216. https://doi.org/10.1016/j.braindev.2009.02.009

12. Connor JR, Menzies SL, Burdo JR et al (2001) Iron and iron management proteins in neurobiology. Pediatr Neurol 25(2):118–129. https://doi.org/10.1016/s0887-8994(01)00303-4

13. George TJ, Beaty CA, Kilic A et al (2012) Hemoglobin drift after cardiac surgery. Ann Thorac Surg 94(3):703–709. https://doi.org/10.1016/j.athoracsur.2012.03.038

14. Kalyani SD, Miller NR, Dong LM et al (2004) Incidence of and risk factors for perioperative optic neuropathy after cardiac surgery. Ann Thorac Surg 78(1):34–37. https://doi.org/10.1016/j.athoracsur.2004.02.015

15. Williams I (2003) Risk factors for ischemic optic neuropathy after cardiopulmonary bypass: a matched case/control study, by GA Nuttall, JA Garrity, JA Dearani, MD Abel, DR Schroeder, and CJ Mullany Anesth Analg 93:1410-6, 2001. Surv Ophthalmol 48(2):237–238. https://doi.org/10.1016/s0039-6257(02)00452-6

16. Ziegler O, Guerci B, Algan M et al (1994) Improved visual evoked potential latencies in poorly controlled diabetic patients after short-term strict metabolic control. Diabetes Care 17(10):1141–1147. https://doi.org/10.2337/diacare.17.10.1141

17. Celesia GG, Daly RF (1977) Effects of aging on visual evoked responses. Arch Neurol 34(7):403–407. https://doi.org/10.1001/archneur.1977.00500190037005

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