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Original Article

Evaluation of medulla spinalis perfusion during aortic arch surgery with antegrade selective cerebral perfusion

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Abstract

Aim: Lower body circulatory arrest with antegrade selective cerebral perfusion (ASCP) during aortic arch surgery can lead to postoperative ischemic spinal cord injury due to the disturbance of blood supply to the cord. Methods that might provide early detection such as near-infrared spectrometry (NIRS) and biomarkers have been evaluated throughout the perioperative phase.
Material and Methods: Thirty consecutive patients were prospectively enrolled in the study. NIRS data were obtained from the cerebral and thoracic spine region. Additionally, S100β protein levels, lactate blood levels and postoperative neurological outcomes were evaluated at various surgery phases.
Results: A total of 30 patients underwent elective hemiarch (73.29%) or total arch (23.31%) replacement with a mean ASCP period of 25.1±19.0 (limits 10-90) minutes. Paraparesis developed in one patient (3.33%). During ASCP period, a significant difference between thoracic T5 and T10 NIRS values was observed (55.40 vs 51.07 respectively, p=0.001).
Conclusion: Thoracic 5th and 10th level NIRS monitoring for spinal cord oxygenation was significantly lower during ASCP period compared to the other periods of aortic arch surgery with T10 values being lower than T5 values during the same period indicating a more significant flow disturbance at this level. Measuring lactate levels with thoracic NIRS monitoring seems promising for future studies.

Keywords: Spectroscopy near-infrared, spinal cord ischemia, S-100B protein human, lactic acid

INTRODUCTION

Antegrade selective cerebral perfusion (ASCP) has a widespread use today for cerebral protection during aortic arch surgery with increasing incorporation of moderate hypothermia (20.1-28°C) during lower body circulatory arrest (LBCA) [1,2]. Despite its benefits, concerns remain about the protection of the spinal cord and distal abdominal viscera during LBCA, as nervous tissue is highly sensitive to ischemia, leading to complications ranging from sensory loss to paraplegia. Studies have shown that blood flow to the spinal cord below thoracic segments 8 and 9 may be insufficient during LBCA with ASCP [3]. This finding has also been confirmed in a pilot study with near infrared spectrometry (NIRS) [4].

Considering that a real time information system may help raise awareness of the team about ischemic damage of the spinal cord during thoracoabdominal interventions where there is a considerably high risk of paraplegia, pioneering experimental works with NIRS yielded acceptable results [5-7]. Feasibility of

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NIRS monitoring of spinal cord in open, endovascular and hybrid thoracoabdominal interventions has also been confirmed [7-9]. The quantity of different metabolites produced as a consequence of neuronal injury due to ischemia in the nervous system increases in both the systemic blood circulation and Cerebrospinal Fluid (CSF) [10]. This study aims to monitor fluctuations in blood levels of s100β (indicative of neuronal damage) and lactic acid (used to assess organ hypoperfusion) during arch surgery, seeking correlations between these metabolites and NIRS measurements of spinal cord oxygenation.

MATERIAL AND METHODS

Patients

Thirty consecutive patients who were to undergo elective ascending and arcus aorta operations by a single surgeon were prospectively evaluated between December 2019 and 2020. Patients younger than 18 years of age, those who were undergoing emergent operation for acute type 1 aortic dissection or those who were receiving antiplatelet-anticoagulant medication were excluded from the study. Demographic parameters, medical history including comorbidities and medications were recorded. Thorough evaluation with echocardiography, carotid-vertebral doppler imaging and computed tomography were performed in all patients. Paraplegia was determined as a complete impairment in motor and sensory function of the lower extremities. Paraparesis refers to partial neurologic dysfunction of the lower extremity. Transient neurologic dysfunction was defined as postoperative confusion, agitation, delirium, or obtundation with a negative brain computed tomography scan and complete resolution before discharge.

Ethical Approval

This article had ethical Approval from the Ethics Committee No:1 of Ankara City Hospital with reference number E1/006/2019.

Patient Consent Statement

Written consent was taken from every patient who contributed to the study.

Surgical Technique

Proximal right brachial artery cannulation with unilateral ASCP and 28°C hypothermia was used in all patients [8,11]. Hypothermia is frequently used, especially in cases where cardiopulmonary bypass is utilized. Although intraoperative monitoring of hypothermia can be performed from many sites, in this study, temperature monitoring was performed simultaneously from both nasopharyngeal and rectal sites. The effectiveness of the nasopharyngeal site in showing cerebral temperature and the rectal site in showing body core temperature led to the preference of these sites. Since there may be different temperature values between the organs during warming and cooling, measurements were taken from two different sites. When the desired values were reached in both sites, ASCP and LBCA were performed. The steps involved in this process can be briefly summarized as follows: While the cross clamp is in place, flow is reduced and clamps are placed on the branches of the arch of aorta. The cross clamp is then removed, allowing for cerebral perfusion to be established and achieved into LBCA state. With the removal of the aortic clamp, the distal part of the aorta is thoroughly explored and an anastomosis line is created, thus performing the open distal anastomosis technique. Back bleeding from left carotid artery was always controlled to test the adequacy of collateral flow from the right carotid system. During ASCP, 700-800 mL/min (10 mL/kg/min) blood flow was provided with cerebral NIRS monitoring (right and left frontal regions). If ASCP period was anticipated to last longer than 40-45 minutes or a difference between right and left cerebral NIRS values with more than 20% drop from the baseline was observed, bilateral perfusion was employed through a separate left carotid artery cannula.

The major surgical techniques used in the study are briefly as follows: For hemiarch surgery, ASCP is completed by performing a distal anastomosis before the innominate artery. In total arch replacement, the aortic arch branches are separated from the aorta, if possible, in the form of an islet. The distal anastomosis is accomplished distal to the left subclavian artery. After the distal anastomosis is performed, the branches are anastomosed to the graft as an islet and the ASCP is terminated.

For spinal cord, rSO2 NIRS monitoring pallets were placed at the skin over spinous process of 5th and 10th thoracic vertebrae level. NIRS values (rSO_2) were measured 1) at baseline before anesthetic induction; 2) at 10th minute when anesthetic induction and hemodynamic stabilization was accomplished; 3) 10 minutes after initiation of cardiopulmonary bypass (CPB); 4) 10 minutes after cross clamp application; 5) at the end of ASCP period; and 6) 10 minutes after conclusion of CPB. (SOMANETICS INVOSTM 7100 Cerebral/Somatic Oximeter, Medtronic) (Minneapolis, USA).

During NIRS monitoring either in carotid endarterectomy, cardiac surgery, or aortic surgery usually more than 20% relative decrease from baseline is considered as an alarm threshold. The Japanese Society of Cardiovascular Anesthesiologists' guideline suggests that a relative rSO_2 decrease of 20 to 36% of baseline is closely associated with neurologic events for cerebral NIRS monitoring during aortic surgery [12]. For the spinal cord there is no such determined critical NIRS cut off value in the literature so both 20 and 36% reductions in rSO_2 values were evaluated in the present study.

Blood Lactate and s100β Measurements

Lactate levels were studied: 1) 10 minutes before induction of ASCP; 2) At the 10^{th} minute of ASCP; 3) following termination of ASCP (in the first 10 minutes, when hemodynamic stabilization was accomplished); 4) in the 2^{nd}; and 5) the 6^{th} postoperative hours from the left radial artery cannula. At the end of ASCP,

an additional blood sample was taken from descending aorta. For s100β determination, blood samples were obtained from descending aorta just before terminating ASCP and from radial artery in the 6th postoperative hour. Kits obtained from Cloud Clone Human ELISA (Texas, USA) were used for s100β determination. All blood samples were centrifuged for 20 minutes with 1000 cycles/minute and the sera obtained were kept at 80°C to be dissolved all at once.

Statistical Analysis

Statistical analyzes were performed using SPSS software version 15. The conformity of the variables to the normal distribution was examined using visual (histogram and probability graphs) and analytical methods (Kolmogorov-Smirnov/Shapiro Wilk tests). Descriptive analyzes were shown using median and minimum-maximum values for non-normally distributed variables. In addition, mean, standard deviation values and ordinal variables were shown using frequency tables. Wilcoxon test was used for in-group rank pairwise comparisons. Friedman test was used to compare data with more than two repetitive measurements. If required, pairwise comparisons were made using the Wilcoxon test and evaluated using Bonferroni correction. Ordinal variables in two related samples were compared with McNemar test. Correlation coefficients and statistical significance for the relationships between parameters were calculated by Spearman's test. The p value was taken as 0.05 for statistical significance.

Data Availability Statement

In order to protect patient privacy, the data are presented in a limited way in the manuscript.

RESULTS

Male patients consisted of the majority (80%) with a mean age of 53.47±15.22 years (Table 1).

Table 1. Demographic and preoperative variables

Variables	Mean±SD (min-max) or No (%) (N=30)
Age (y)	53.5±15.2 (22-78)
Male sex	24 (80)
Body mass index (kg/m²)	26.3±3.9 (19.5-35.9)
Coronary artery disease	11 (36.7)
History of cerebrovascular disease	1 (3.3)
Diabetes mellitus	4 (13.3)
Chronic obstructive pulmonary disease	1 (3.3)
Aortic pathology	30 (100)
Aneurysm	28 (93.3)
Chronic dissection	2 (6.66)
Previous cardiovascular surgery	4 (13.3)

Total arch replacement was performed in 7 patients and in 1 patient arch graft revision for aortic valve endocarditis was performed. There were 22 patients who received hemiarch replacement. Aortic valve replacement was the most frequently associated procedure (40%) followed by coronary artery bypass grafting (CABG) (23.3%), Bentall procedure (13.3%) and valve sparing root replacement (10%). There were 4 reoperations (13.3%) and 2 patients with subacute and chronic aortic dissection. Surgical procedures and intraoperative data are shown in Table 2.

Hospital mortality was 6.7% with two patients. The aforementioned patients were lost during the postoperative phase, and subsequent monitoring revealed no signs of spinal cord ischemia.

Table 2. Surgical procedures and intraoperative variables

Variables	Mean±SD (min-max) or No (%) (N=30)
Aortic arch reconstruction	30 (100)
Hemi arch	22 (73.3)
Total arch	7 (23.3)
Aortic arch revision	1 (3.3)
Elephant trunk	2 (6.7)
Bentall procedure	4 (13.3)
Valve sparing aortic root replacement	3 (10)
Coronary artery bypass grafting	7 (23.3)
Aortic valve replacement	12 (40)
Operative variables	
CPB time (min)	192.6±64.0 (105-371)
Aortic cross clamp time (min)	113.5±33.0 (45-187)
ASCP time (min)	25.1±19.0 (10-90)
MAP–ASCP (mmHg)	49.5±14.0 (15-70)
SaO_2–ASCP (%)	98.2±0.5 (97-99)
Hct–ASCP (%)	25.6±4.8 (14-33)

ASCP: antegrade selective cerebral perfusion, CPB: cardiopulmonary bypass, Hct: hematocrit, MAP: mean arterial pressure, SD: standard deviation

ASCP perfusion was unilateral in 27 patients (90%). Bilateral cerebral perfusion was administered in 3 patients (10%, ASCP periods of 64, 90, and 63 minutes) all of whom survived with one patient suffering from paraparesis (3.3%). The mean ASCP duration of all patients was found to be 25.13±19.02 minutes (range 10-90 minutes). This patient suffering from paraparesis had ascending and total arch replacement with distal elephant trunk formation due to subacute type I aortic dissection after a

primary percutaneous coronary intervention a month ago. The total ASCP duration was 90 minutes, 57 minutes of which was performed as bilateral cerebral perfusion. He also had transient neurologic dysfunction (agitation and mild obtundation) and his motor function deficit was graded as 4/5 with no evidence of sensory loss. There was no significant reduction in cerebral NIRS values (7.5% and 13% reduction in his right and left cerebral NIRS values respectively). But his T10 rSO_2 NIRS level dropped by 34.7% in the 33rd minute and regressed to 22.2% with administration of bilateral ASCP. No other permanent neurologic deficit was observed in any other patient.

In the whole group, there was a slight decline in right and left cerebral NIRS values from the onset of CPB until the end of CPB in the whole group, but this difference did not reach to significance in any period ($p<0.05$). Regarding T5 and T10 NIRS values, most significant reductions occurred during the ASCP period. They started to decrease gradually with the onset of CPB, dropped significantly with cross clamp application, being lowest during ASCP ($p<0.001$) (Figure 1). T10 levels were also significantly lower than T5 levels during the same period (51.07±12.76 vs 55.40±9.21 respectively, p=0.001). More than 20% reduction was observed in 17 patients' T5 NIRS values (56.7%, $p<0.001$), and 22 patients' T10 values (73.3%, $p<0.001$). The patient with paraparesis was in this group. A drop more than 36% of baseline occurred less frequently during the same period (in 1 patient's T5 and in 7 patients' T10 NIRS values, p=1.00 and p=0.016 respectively) without any neurologic event. The only patient with more than 36% reduction in both T5 and T10 NIRS values had only 17 minutes of ASCP without any postoperative neurologic complication.

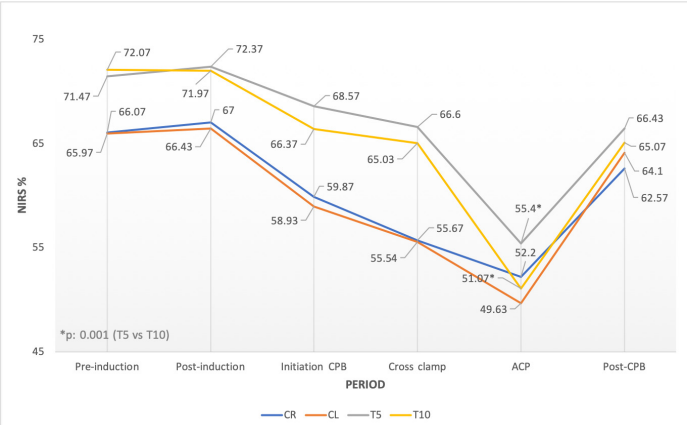

Figure 1. Periodic distribution of NIRS data from CR, CL, T5 and T10 regions; ACP: antegrade cerebral perfusion, CPB: cardiopulmonary bypass

There was a good correlation between T5 and T10 NIRS values during ASCP period ($r=0.853$, $p<0.001$) but we could not detect any correlation between the cerebral and thoracic NIRS values during the same period (CR-T5 r=0.345, p=0.062 and CL-T5 r=0.344, p=0.062).

s100β levels at the postoperative 6th hour fell significantly with respect to the period corresponding to the end of ASCP (2.086±0.971 vs 1.082±0.82; $p<0.001$) (Table 3).

Table 3. Perioperative data of S100β and lactate

		Mean±SD	p
S100β (ng/mL)	**End of ASCP (descending aorta)**	2.09±0.97	p<0.001
	Postoperative 6th hour	1.08±0.83	
Lactate (mmol/L)	**Pre-ASCP**	$3.21\pm1.76^{\Omega,\Sigma}$	$p^{\Omega}=0.002$
	During ASCP	$3.86\pm1.61^{\Omega,\Psi,\alpha}$	$p^{\Psi}<0.001$
	Post-ASCP	$6.77\pm2.38^{\Psi,\Sigma}$	
	Postoperative 2nd hour	$5.96\pm2.53^{\Sigma}$	$p^{\Sigma}<0.001$
	Postoperative 6th hour	$5.55\pm2.23^{\Sigma}$	
	End of ASCP (descending aorta)	$4.52\pm1.56^{\alpha}$	$p^{\alpha}=0.002$

ACP: antegrade selective cerebral perfusion, SD: standard deviation, p^{Ω}: p value of lactate levels in Pre-ACP and during ACP, p^{Ψ}: p value of lactate levels in during ACP and Post-ACP, p^{Σ}: p-value of lactate levels in Pre-ACP, postoperative 2nd and 6th hour, p^{α}: comparison of blood lactate values taken from the descending aorta and radial artery during ACP

Lactate levels increased with the onset of ASCP reaching their highest level with the termination of ASCP and diminishing afterwards in the postoperative period with significant difference compared to each preceding period ($p^{\Sigma}<0.001$, Table 3, Figure 2). Lactate levels in blood samples obtained from descending aorta at the end of ASCP were significantly higher than the samples drawn during ASCP from the radial artery with a moderately positive correlation between them (4.52±1.56 vs 3.86±1.61 respectively, p=0.002 and r=0.655, $p<0.001$).

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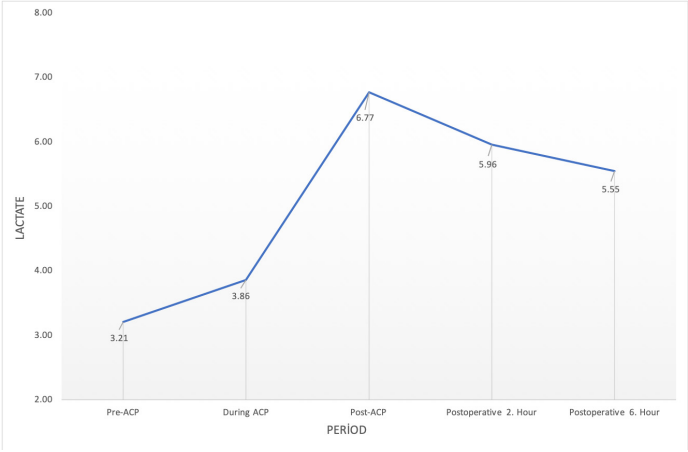

Figure 2. Periodic distribution of lactate levels; ACP: antegrade cerebral perfusion

No correlation was observed between s100β, lactate levels, T5 and T10 thoracic NIRS values at the end of the ASCP period (r=0.202, p=0.284 and r=-0.040, p=0.833 respectively). On the other hand, there was moderate negative correlation between lactate levels of descending aorta and T10 NIRS values during the same period (r=-0.514, p=0.004) (Figure 3).

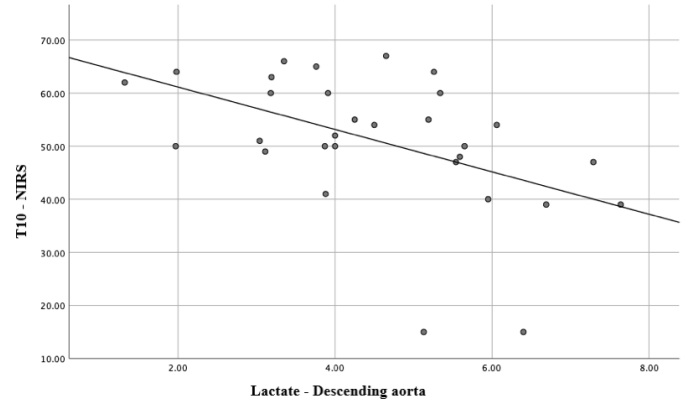

Figure 3. Correlation of NIRS data from T10 level with lactate values in blood sample from descending aorta during ASCP

DISCUSSION

The implementation of NIRS for monitoring spinal cord perfusion during aortic arch surgery presents a valuable opportunity to enhance patient safety by effectively identifying potential spinal cord ischemia. However, NIRS reflects mixed tissue oxygenation rather than absolute values, and a decrease of 20–30% from the reference level suggests a possible risk of ischemia. In patients undergoing arch replacement optodes placed at the 3rd and 10th thoracic vertebra over the paraspinous muscles, Kinoshita et al. displayed a significant fall in regional oxygen saturations with the start of ASCP. While T10 values continued to decrease to about 20% of baseline, T3 NIRS levels remained relatively stable [4]. In the present study, T10 NIRS values tend to be lower than the T5 levels in each period and this difference was significant during the ASCP period, reflecting less perfusion of the lower part of the spinal cord. More than half of the patients experienced over 20% drop in T5 and T10 levels and only one of them had postoperative paraparesis. None of the patients with more than a 36% drop in their baseline NIRS values during ASCP suffered from paraplegia. The time period during which NIRS values remain low is very important, but we do not have this data which is one of the limitations of the present study.

One important finding of the present study is negative correlation between the lactate levels in descending thoracic aorta and T10 NIRS values during the ASCP period. Lactate levels that were retrieved during ASCP from the radial artery and descending aorta were moderately correlated (r=0.655), but they were significantly higher in descending aorta probably due to the retrograde blood flow to descending aorta from the visceral, thoracic and lumbar arteries rich in lactate. The decrease in NIRS data during LBCA and the rise in lactate levels from the descending aorta may indicate early cord damage. Measuring lactate alongside T10 NIRS monitoring during open distal anastomoses could be useful in arch operations with long ASCP periods. However, studies with larger volumes may help to determine a threshold limit to be used as an alarming sign for spinal cord ischemia.

Spinal cord perfusion is maintained by segmental arteries from the thoracic and abdominal aorta and increased with the contribution of left subclavian, intercostal, lumbar, hypogastric arteries and the local paraspinous arterial tree embedded in the paraspinous muscles according to the current collateral network concept. As ASCP eliminates the segmental and hypogastric artery contribution to the spinal cord blood supply, it is suggested that nearly two thirds of total flow is lost leaving the vertebral and intercostal arteries only to perfuse the cord [8,13-15]. Therefore, when additional distal perfusion is not used, duration of ischemic period and the degree of hypothermia become the critical issues for spinal cord protection during arch surgery.

There is no consensus as to the safe duration of ASCP to rule out spinal cord ischemic injury during arch surgery with lower body circulatory arrest. As most reports are based on experimental studies, concerns about safe period remain [3,16-18]. Spinal cord injury was inevitable after 120 minutes and probable after 90 minutes in an experimental study at 28°C. At temperatures of 25-28°C, when LBCA>60 minutes, a trend towards higher paraplegia rate was found compared to temperatures between 20-24.9°C (18.2% vs 0%, p=0.08) [19]. Paraplegia rates are usually 5 to 8% in contemporary series [19,20]. Zierer et al. reported 0.3% paraplegia rate in 1002 patients operated at 26-34°C and mostly unilateral ASCP (67.2%). Aortic dissection was the shared pathology in all paraplegic patients with a wide range of ASCP periods (24, 41 and 127 minutes) [21]. Occurrence of paraplegia was also attributed to the creation of elephant trunk

as it may cause a delay for reperfusion injury or inadequate perfusion [22]. In a pioneering study conducted by Kinoshita et al., no paraplegia was observed in patients undergoing arch replacement at 24-26°C core temperature [4]. Mean lower body circulatory arrest durations were longer compared to our study (49±14 vs 25.13±19.02 minutes) but not longer than 90 minutes in any patient (ranges between 24 and 72 minutes) owing to addition of lower body circulation via a side branch from the graft. Mean ASCP duration was relatively short (25.13±19.02 minutes) in the present study (range 10-90 min) with 3 patients' duration exceeding 60 minutes (63, 64 and 90 minutes). The only patient in the present study with postoperative paraparesis (3.3%) had previous chronic aortic dissection, 90 minutes of ASCP and elephant trunk formation consistent with the above-mentioned studies. We can conclude that when LBCA durations are expected to approach 90 minutes or over, additional lower body perfusion should be implemented after 60 minutes [3].

Regarding s100β levels, in patients with spinal cord injury after thoracoabdominal operations, Kunihara et al. observed that serum levels reached peak levels just after the operation and patients with spinal cord injury had a second peak at 24 hours postoperatively (1.3±1.4 μg/L) [10]. We do not have a baseline s100β value preoperatively, but the values in 6th postoperative hour fell significantly compared to values at the end of ASCP. Our values are somewhat higher, but serious neurological complication occurred in one patient whose s100β levels were 0.33 ng/mL and 1.929 ng/mL respectively and one patient is not enough to make a reliable statistical evaluation.

One of the most important drawbacks of the present study is the failure to monitor lumbar spine NIRS values. We could have observed a significant fall in lumbar NIRS values before any reduction occurred in the thoracic level. Another shortcoming is the absence of basal s100β level determination before any procedure took place. Another limitation of the study is that patients with acute aortic dissection were excluded, but there were 2 patients with chronic aortic dissection with previous intervention to the ascending aorta and aortic valve. Instantaneous display of NIRS during the operation was available; however, we could not record them. This study was conducted in a small patient group. Large scale studies are needed to arrive at a better conclusion regarding alarming signs for spinal cord injury during aortic arch surgery.

CONCLUSION

In conclusion, this study focuses on the importance of monitoring spinal cord perfusion during aortic arch surgery, especially when using ASCP and LBCA. Our findings indicate that prolonged ASCP, particularly beyond 60 minutes, raises the risk of ischemic injury to the spinal cord, showing the need for additional strategies in high-risk cases. Furthermore, the risk of ischemia increases in direct proportion to the ASCP duration, the utilization of NIRS and lactate data can be stated as a viable approach for establishing an early warning system during aortic arch surgery. Consequently, enhanced monitoring strategies are required to minimize the risk of devastating complications such as paraplegia in patients undergoing aortic arch surgery.

Ethics Committee Approval: This article had ethical Approval from the Ethics Committee No: 1 of Ankara City Hospital with reference number E1/006/2019.

Patient Consent for Publication: Written consent was obtained from participating patients.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: All authors contributed equally to the article.

Conflict of Interest: The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

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