

Comparison of cases with and without additional lower body perfusion in newborns undergoing aortic arch reconstruction with antegrade selective cerebral perfusion method

Antegrad selektif serebral perfüzyon yöntemi ile aortik ark rekonstrüksiyonu yapılan yenidoğanlarda ilave alt vücut perfüzyonu yapılan ve yapılmayan olguların karşılaştırılması

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ABSTRACT

Background: The aim of this study was to analyze the effect of additional lower body perfusion, compared to antegrade selective cerebral perfusion, on early postoperative outcomes after aortic arch repair in neonates with biventricular morphology.

Methods: Between January 2017 and April 2020, a total of 46 neonates (34 males, 12 females; median age: 10 days; range, 7 to 14 days) with biventricular morphology underwent an aortic arch reconstruction were retrospectively analyzed. The effects of antegrade selective cerebral perfusion and additional lower body perfusion techniques on vital organ preservation and mortality were evaluated in these patients who underwent arch reconstruction.

Results: In the univariate analysis of the whole cohort, postoperative creatinine level was lower in the additional lower body perfusion group, while there was no significant difference between the other parameters. In the multivariate analysis, intraoperative highest lactate level (odds ratio: 1.7; 95% confidence interval: 1.07-2.68; p=0.02) and postoperative 4th to 6th h lactate levels (odds ratio: 2.34; 95% confidence interval: 1.08-5.09; p=0.03) were independent predictors of early mortality. Mortality rate was higher in the antegrade selective cerebral perfusion group (22% vs. 7%), although it did not reach statistical significance. In the receiver operating characteristic curve analysis, the cut-off value for intraoperative lactate was 6.2 mmol/L (sensitivity: 85.7%, specificity: 71.1%) and the cut-off value for the lactate level at the postoperative 4th to 6th h was 4.9 mmol/L (sensitivity: 85.7%, specificity: 73.7%). Above these lactate levels were found to be associated with mortality.

Conclusion: Additional lower body perfusion may have a role in vital organ protection in aortic arch repair of neonates, compared to antegrade selective cerebral perfusion.

Keywords: Aortic arch repair, cannulation technique, descending aortic cannulation.

ÖZ

Amaç: Bu çalışmada biventriküler morfolojiye sahip yenidoğanlarda aortik ark onarımı sonrası erken ameliyat sonrası sonuçlara ilave alt vücut perfüzyonunun antegrad selektif serebral perfüzyona kıyasla etkisi incelendi.

Çalışma planı: Ocak 2017 - Nisan 2020 tarihleri arasında aortik ark rekonstrüksiyonu yapılan biventriküler morfolojiye sahip toplam 46 yenidoğan (34 erkek, 12 kız; medyan yaş: 10 gün; dağılım 7-14 gün) retrospektif olarak incelendi. Ark rekonstrüksiyonu yapılan bu hastalarda antegrad selektif serebral perfüzyon ve ilave alt vücut perfüzyonu tekniklerinin hayati organ koruma ve mortalite üzerine etkileri değerlendirildi.

Bulgular: Tüm kohortun tek değişkenli analizinde, ameliyat sonrası kreatinin düzeyi ilave alt vücut perfüzyon grubunda daha düşük iken, diğer parametreler arasında anlamlı bir fark yoktu. Çok değişkenli analizde ameliyat sonrası en yüksek laktat düzeyi (risk oranı: 1.7; %95 güven aralığı: 1.07-2.68; p=0.02) ve ameliyat sonrası 4 ila 6. saat laktat düzeyleri (risk oranı: 2.34; %95 güven aralığı: 1.08-5.09; p=0.03), erken mortalitenin bağımsız öngördürücüleri idi. Mortalite oranı, antegrad selektif serebral perfüzyon grubunda daha yüksek olup (%7'ye kıyasla %22), istatistiksel olarak anlamlı değildi. Alıcı işletim karakteristik eğrisi analizinde, ameliyat sonrası laktat için eşik değeri 6.2 mmol/L (duyarlılık: %85.7, özgüllük: %71.1); ve ameliyat sonrası 4 ila 6. saat laktat düzeyinin eşik değeri 4.9 mmol/L (duyarlılık: %85.7, özgüllük: %73.7) idi. Bu laktat düzeylerinin üstü mortalite ile ilişkili bulundu.

Sonuç: İlave alt vücut perfüzyonu, antegrad selektif serebral perfüzyona kıyasla, yenidoğanların aortik ark onarımında hayati organ korumasında rol oynayabilir.

Anahtar sözcükler: Aortik ark onarımı, kanülasyon tekniği, inen aort kanülasyonu.

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Aortic arch anomaly has a high surgical risk in neonates.^[1,2] When the proximal arch is involved, the procedure of choice is repair through median sternotomy under cardiopulmonary bypass (CPB). The perfusion strategies commonly in use are hypothermic circulatory arrest (HCA) and antegrade selective cerebral perfusion (ASCP).

Recently, whole body perfusion by descending aortic cannulation is under investigation to reduce the risk of organ damage during this procedure. There have been a limited number of reports claiming the superiority of additional lower body perfusion (ALBP) in organ protection compared to ASCP.^[3-6]

In the present study, we aimed to compare the early postoperative outcomes after aortic arch and intracardiac surgical repairs in neonates with biventricular physiology between the patients who were operated under ASCP and ALBP.

PATIENTS AND METHODS

This single-center, retrospective study was conducted at Department of Pediatric Cardiac Surgery, Dr. Siyami Ersek Thoracic and Cardiovascular Surgery Training and Research Hospital, between January 2017 and April 2020. A total of 46 neonates (34 males, 12 females; median age: 10 days; range, 7 to 14 days) who underwent procedures that involved aortic arch repair through a median sternotomy were included. Exclusion criteria were as follows: univentricular physiology and preoperative mechanical ventilation. Data were retrieved from the hospital database. The primary outcome measures were early postoperative blood urea nitrogen (BUN), creatinine (Cr), and lactate levels. These values were sampled on intensive care unit (ICU) admission. Other parameters compared between the groups were early postoperative hematocrit (hct), postoperative lactate levels at 4 to 6 h of surgery, the use of peritoneal dialysis, delayed sternal closure, postoperative extracorporeal membrane oxygenation (ECMO), reoperation, postoperative lengths of mechanical ventilation (days), ICU stay (days), hospital stay (days), and hospital mortality.

For secondary outcomes, the whole cohort was used to analyze risk factors associated with hospital mortality. The risk factors analyzed were as follows: (i) preoperative parameters such as age, height, weight, sex, body surface area, renal failure, hct, BUN, Cr, lactate levels (taken before beginning of surgery); (ii) intraoperative parameters such as CPB time, aortic cross-clamp (ACC) time, ASCP time, intraoperative highest lactate level, heat, and hct; (iii) postoperative parameters such as the use of peritoneal dialysis,

length of hospital stay, ICU stay (days), postoperative hct, BUN, Cr, lactate levels (between 4th and 6th h of surgery), delayed sternal closure, postoperative ECMO, reoperation, mechanical ventilation time (days), and hospital mortality.

Operative technique and CPB protocol

After median sternotomy, the thymus was excised and the pericardium was harvested. The aortic arch with its branches, the arterial duct and the descending aorta were mobilized. The arch vessels were looped with elastic snares. The brachiocephalic artery was cannulated (DLP; Medtronic, Grand Rapids, MI, USA). Superior and inferior caval veins were cannulated, and CPB was initiated.

In the ASCP group, no further vessels were cannulated. The patient was cooled down to 28°C. Right after ACC and Del Nido cardioplegia infusion, ASCP was established by snaring the arch vessels and clamping the descending aorta. The pump flow was reduced 50 to 100 mL/kg/min to maintain the right radial artery pressure at 40 to 60 mmHg during arch

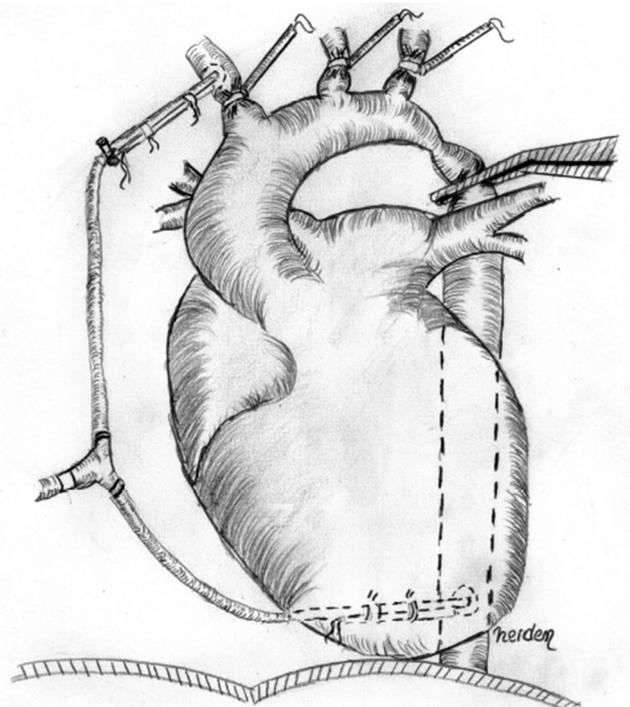


Figure 1. Cannulation technique: The arch vessels were looped with elastic snares. The brachiocephalic artery was cannulated. Superior caval vein was cannulated (not shown), and cardiopulmonary bypass was initiated. The descending aorta at the level of diaphragm was cannulated right after institution of the cardiopulmonary bypass. Then inferior caval vein was cannulated (not shown).

repair. After the arch reconstruction and de-airing, snares of the arch vessels and the clamp on the descending aorta were removed. Full-flow CPB was resumed and continued for the rest of the operation.

In the ALBP group, the descending aorta at the level of diaphragm was cannulated right after institution of the CPB. For this cannulation, apex of the heart was retracted cephalad by the help of the pump-sucker. Posterior pericardium was incised longitudinally. The descending aorta was dissected free and then cannulated directly. This cannula was Y-connected to the brachiocephalic artery cannula. Under full-flow CPB, the patient was cooled down to 32°C (Figure 1). After the ACC and Del Nido cardioplegia infusion (Figure 2), the arch vessels were snared and the descending aorta was clamped. The arch was reconstructed under full-flow CPB. After the reconstruction, snares of the arch vessels and the clamp on the descending aorta were removed. The rest of the operation was completed. The descending aortic cannula was removed after removal of the ACC. We used aortic arch reconstruction with an autologous pericardial patch and aortic arch advancement techniques for arch repair.^[7,8]

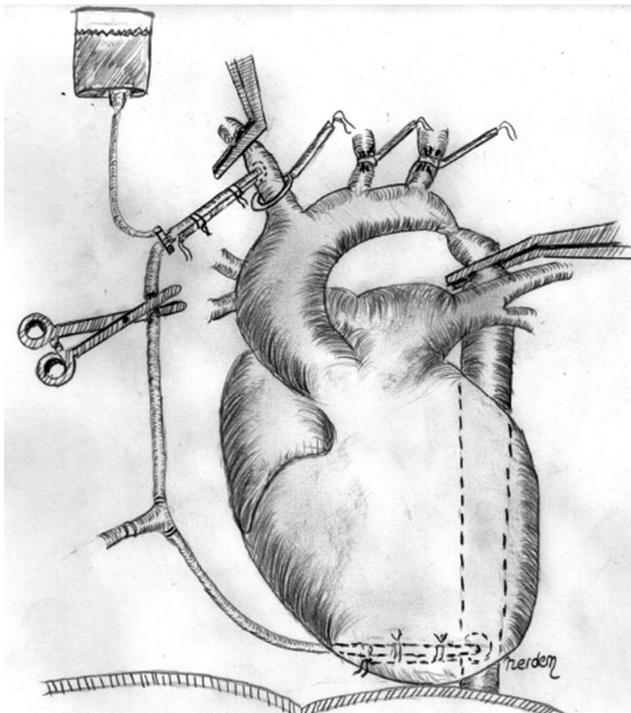


Figure 2. Cardioplegia technique: The innominate artery is cross-clamped distal to the cannula, and Del Nido cardioplegia solution is infused via the aortic cannula, while cardiopulmonary bypass is off for a short time.

Table 1. Baseline characteristics of patients

	ASCP (n=32)			ALBP (n=14)			Cohort (n=46)		
	n	%	IQR	n	%	IQR	n	%	IQR
Age (day)			8-15			6-13			7-14
Sex									
Male	26			8			34		
Female	6			6			12		
Height (cm)			49-52			50-51			50-52
Weight (kg)			2.9-3.5			3.0-3.7			2.9-3.6
Body surface area (m ²)			0.20-0.22			0.20-0.23			0.20-0.23
Preoperative blood tests									
Blood urea nitrogen			7			6			6
Creatinine			0.47			0.50			0.48
Hematocrit			38			44			40
Lactate			1.5			2.0			1.6
STAT mortality category									
4	31	97		14	100		45	98	
5	1	3		0	0		1	2	

ASCP: Antegrade selective cerebral perfusion; ALBP: Additional lower body perfusion; IQR: Interquartile range; STAT: Society of Thoracic Surgeons-European Association for Cardio-Thoracic Surgery.

Table 2. Intraoperative parameters

	ASCP (n=32)		ALBP (n=14)		<i>p</i>
	Median	IQR	Median	IQR	
Intraoperative hematocrit	38	36-41	37	36-40	>0.05
Heat	28	28-32	32	32-32	0.006
Intraoperative highest lactate	6.2	4.9-10.9	5.0	3.2-5.2	0.005
CPB time (min)	151	119-205	123	77-144	0.031
Cross-clamp time (min)	84	64-113	61	0-78	0.019
ASCP time (min)	47	27-54	-	-	>0.05

ASCP: Antegrade selective cerebral perfusion; ALBP: Additional lower body perfusion; IQR: Interquartile range; CPB: Cardiopulmonary bypass.

Statistical analysis

Statistical analysis was performed using the IBM SPSS version 21.0 software (IBM Corp., Armonk, NY, USA). Continuous data were presented in median (interquartile range [IQR]), while categorical data were presented in number and frequency. The two groups were compared using the chi-square or Fisher exact tests for categorical variables and Mann-Whitney U test for continuous variables. Binary logistic regression was used to analyze risk factors of in-hospital mortality. The predictive power of the independent risk factors of in-hospital mortality were analyzed using the receiver operating characteristic (ROC) curves. A *p* value of <0.05 was considered statistically significant.

RESULTS

Table 1 summarizes baseline characteristics of the patients. The whole cohort was divided into two groups as ALBP and ASCP. There was no significant difference between the baseline parameters except for preoperative htc, which was higher in the ALBP group. Two (6%) patients in the ASCP group and one (7%) patient in the ALBP group required peritoneal dialysis preoperatively.

Table 2 shows the comparison of the intraoperative parameters between the groups. The CPB time and ACC time were shorter and body temperature was higher in the ALBP group. Intraoperative lactate levels were higher in the ASCP group.

Table 3. Postoperative parameters

	ASCP (n=32)				ALBP (n=14)			
	n	%	Median	IQR	n	%	Median	IQR
Postoperative BUN			7	5-11			6	5-8
Postoperative creatinine			0.58	0.51-0.68			0.50	0.46-0.58
Postoperative hematocrit			40	36-45			41	37-43
Postoperative lactate (4-6 h)			4.6	2.7-5.4			3.7	2.4-5.2
Peritoneal dialysis	4	12			1	7		
Delayed sterna closure	18	56			6	42.9		
Postoperative ECMO	7	22			1	7		
Reoperation	5	16			2	14		
Mechanical ventilation (days)			6	4-14			4	3-5
ICU stay (days)			9	7-26			8	6-9
Hospital stay (days)			13	9-28			12	9-17
Hospital mortality	7	22			1	7		

ASCP: Ante-grade selective cerebral perfusion; ALBP: Additional lower body perfusion; BUN: Blood urea nitrogen; ECMO: Extracorporeal membrane oxygenation; ICU: Intensive care unit.

Table 4. Factors associated with mortality

	<i>p</i>	Odds ratio	95% CI for OR	
			Lower	Upper
CPB time (min)	0.010	1.026	1.006	1.047
Postoperative creatinine	0.014	60260.359	9.536	380781070.315
Intraoperative lactate	0.005	1.469	1.122	1.923
Postoperative LAC (4-6 h)	0.013	2.114	1.174	3.805
Second CPB	0.021	10.800	1.434	81.330
Postoperative ECMO	0.000	54.000	6.340	459.915

CI: Confidence interval; OR: Odds ratio; CPB: Cardiopulmonary bypass; ECMO: Extracorporeal membrane oxygenation.

Ten (71%) patients in the ALBP group and 24 (75%) patients (one of the patients in the ASCP aortic arch repair group also had aortic and mitral valve repair) in the ASCP group had intracardiac surgery in addition to aortic arch repair. One patient (3%) in the ASCP group previously underwent aortic arch repair. One (7%) patient in the ALBP group and four (12%) patients in the ASCP group required CPB for the second time.

Postoperative Cr ($p=0.037$) level was lower in the ALBP group and there was no significant difference between the other parameters. The mortality rate was higher in the ASCP group (22% vs. 7%); however, the difference did not reach statistical significance ($p>0.05$) (Table 3). The median lengths of mechanical ventilation, ICU stay, and hospital stay were five (range, 3-10) days, eight (range, 6-15) days, and 13 (range, 9-19) days, respectively.

In the univariate analysis of the whole cohort, factors associated with mortality were CPB time (odds ratio [OR]: 1.02; 95% confidence interval [CI]: 1.02-1.0; $p=0.01$), postoperative Cr (mg/dL) (OR: 60260.35; 95% CI: 9.53-380781070.31; $p=0.014$), intraoperative highest lactate (mmol/L) level (OR: 1.46; 95% CI: 1.12-1.92; $p=0.005$), postoperative 4th to 6th h of lactate (mmol/L) level (OR: 2.11; 95% CI: 1.17-3.8; $p=0.013$), second CPB (OR: 10.8; 95% CI: 1.43-81.33; $p=0.021$), postoperative ECMO (OR: 54; 95% CI: 6.34-459.91; $p=0.00$) (Table 4). In the multivariate analysis, intraoperative highest lactate (mmol/L) level (OR: 1.7; 95% CI: 1.07-2.68; $p=0.02$) and postoperative 4th to 6th h of lactate (mmol/L) level (OR: 2.34; 95% CI: 1.08-5.09; $p=0.03$) were independent predictors of early mortality.

In the ROC curve analysis, the cut-off value for intraoperative lactate was 6.2 mmol/L (sensitivity: 85%, specificity: 71%). The cut-off value for the lactate

level at the postoperative 4th to 6th h was 4.9 mmol/L (sensitivity: 85%, specificity: 73%).

DISCUSSION

In our single-center study where we compared ALBP with ASCP and retrospectively examined newborns with biventricular morphology undergoing aortic arch repair, the highest intraoperative lactate level and postoperative Cr level were found to be significantly lower in the ALBP group, compared to the ASCP group. In addition, lactate level at the postoperative 4th to 6th h was also lower in the ALBP group. In the analysis of the whole group, the intraoperative lactate level being 6.2 mmol/L and the postoperative lactate level at 4th to 6th h being higher than 4.9 mmol/L were independently associated with hospital mortality.

The significantly lower intraoperative lactate and postoperative Cr levels in the ALBP group indicate a potential role of this perfusion strategy in vital organ protection during arch repair. Postoperative high Cr levels, as well as intra- and postoperative blood lactic acid levels, are important markers of end-organ failure.^[9,10] Hammel et al.^[5] found that multisite arterial perfusion, including ALBP, and maintenance of continuous mildly hypothermic full-flow CPB might offer advantages as a perfusion strategy for neonatal arch reconstruction. In their study, there was no significant difference in hospital mortality between the HCA/ASCP and the ALBP groups. Also, they analyzed Cr changes compared to baseline. They observed greater loss of glomerular filtration rate in the HCA/ASCP group than the ALBP group at each of the first five postoperative days. These are consistent with our results.

In our study, ALBP was achieved with double arterial cannulation during arch repair in newborns.

There are also other partial lower body perfusion or whole body perfusion techniques which are used for this purpose. For instance, Rajagopal *et al.*^[9] used femoral arterial line or umbilical artery catheter connected to the arterial cannula. Although they reported reduced incidence of acute kidney injury, there was no significant difference in ICU length of stay. Duebener *et al.*^[11] used a larger sheath to place in femoral artery and reached higher flow rates. They reported lower serum lactate and Cr levels postoperatively without a significant difference in clinical outcomes. In these techniques, percutaneously inserted catheters were used and the flow rate limits were related to the diameter of these catheters. Raees *et al.*^[12] inserted a cannula into the lumen of opened descending aorta. Although they found a higher glomerular filtration rate and no significant difference in clinical outcome, the surgeon had to work with a cannula at the site of anastomosis in this technique. This is not a comfortable situation. Yasui *et al.*,^[13] and Fernandez-Doblas *et al.*^[14] used tube graft placed to the descending aorta by left thoracotomy for ALBP. In our technique of ALBP, we directly cannulated descending aorta through median sternotomy. Our highest intraoperative lactate level, postoperative 4th to 6th h lactate level, was significantly lower compared to the ASCP group. Low intra- and postoperative lactate levels indicate minimal end-organ damage and less risk of postoperative serious events.^[10,15] Kreuzer *et al.*^[16] also found similar results in their single-center, retrospective study including 407 consecutive pediatric patients who underwent aortic arch reconstruction under double-arterial cannulation. This is also consistent with the finding that intra- and postoperative 4th to 6th h lactate level is an independent predictor of early mortality. Böttcher *et al.*,^[17] in their study, reported that the use of moderate hypothermia with distal aortic perfusion was associated with a significantly lower incidence of kidney injury. On the other hand, Kulyabin *et al.*^[18] reported that double arterial cannulation did not reduce the acute kidney injury incidence, compared to deep HCA. Our aim was to prevent end-organ damage and to create a psychologically comfortable environment for the surgeon, independent of time anxiety. Boburg *et al.*^[19] used an arterial sheath that was introduced through the femoral artery to achieve a lower body perfusion and the patients did not show a significant increase in lactate, Cr, and liver enzyme levels. Based on our study results, it is wise to prefer ALBP to ASCP in aortic arch repair, particularly for newborns with prolonged distal ischemia, as it reduces lactate levels.

There are several limitations to this study. Our data are limited as it included only 46 patients undergoing

aortic arch repair at a single center. In this cohort, we collected several parameters related to mortality and morbidity. The absence of aortic Z-scores, vasoactive inotrope score of each patient, detailed mortality causes of ECMO patients or retrospective imagining for possible neurological disorders may have limited the significance of the data.

In conclusion, our study demonstrates that aortic arch repair under additional lower body perfusion is safe in neonates with biventricular physiology. The findings that the intraoperative lactate and postoperative creatinine were significantly lower in the additional lower body perfusion group indicate a potential role of this perfusion strategy in vital organ protection during arch repair. This is also consistent with the finding that the intra- and postoperative 4th to 6th h lactate levels were independent predictors of early mortality. This data suggests that, in the absence of randomized-controlled trials, it is prudent to prefer whole body perfusion over antegrade selective cerebral perfusion in aortic arch repair of neonates, particularly if the anticipated ischemic period for the lower body is long.

Ethics Committee Approval: The study protocol was approved by the Dr. Siyami Ersek Thoracic and Cardiovascular Surgery Training and Research Hospital Institutional Review Board (IRB No: 28001928-604.01). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patient Consent for Publication: A written informed consent was obtained from the parents and/or legal guardians of the patients.

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

Author Contributions: Conceptualization - A.Ş., O.K., Y.K.; Data curation - A.S., H.C.; Formal analysis - O.K., M.Ç., Y.K.; Investigation - O.K., Y.K.; Methodology - A.Ş., O.K., Y.K.; Project administration - O.K., F.A., Y.K.; Resources - Y.K., H.C.; Software - O.K., Y.K., H.C.; Supervision - A.S., N.A.A.; Validation - Y.K.; Visualization - H.E., Y.K.; Writing - Original draft - O.K., Y.K.; Writing - Review & Editing - Y.K.

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