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Original Article / Özgün Makale

Factors affecting long-term survival of patients undergoing aortic surgery using the antegrade selective cerebral perfusion technique

Antegrad selektif serebral perfüzyon tekniği ile aort cerrahisi yapılan hastalarda uzun dönem sağkalımı etkileyen faktörler

Anıl Özen,[1] Garip Altıntaş,[1] Ümit Kervan,[1] Ertekin Utku Ünal,[1] Metin Yılmaz,[1] Selin Özen,[2] Zafer İşcan,[1] Mehmet Ali Özatik[3]

Institution where the research was done:
Department of Cardiovascular Surgery, Türkiye Yüksek İhtisas Training and Research Hospital, Ankara, Turkey

Author Affiliations:
[1]Department of Cardiovascular Surgery, Türkiye Yüksek İhtisas Training and Research Hospital, Ankara, Turkey
[2]Department of Physical Medicine and Rehabilitation, Medical Faculty of Ankara University, Ankara, Turkey
[3]Department of Cardiovascular Surgery, Acıbadem Eskişehir Hospital, Eskişehir, Turkey

Background: This study aims to investigate the factors effecting long-term survival of patients undergoing ascending and arcus aortic aneurysm repair and/or dissection surgery using the antegrade selective cerebral perfusion (ASCP) technique.

Methods: Between January 2000 and December 2008, 154 operative survivors of 177 patients (89 males, 65 females; mean age 54.5±12.4 years; range 20 to 84 years) who were operated in our clinic using the ASCP technique and discharged from the hospital were included in the study. Eighty-four patients (54.5%) underwent dissection repair, while 70 (45.5%) underwent aneurysm repair. Patients who survived during the follow-up period were classified as group 1 and those who died were classified as group 2.

Results: The mean follow-up period was 50.5±26.8 (range 3-106) months. Ten patients died during the follow-up period. The mortality rate was 6.49%. The length of intensive care unit stay ($p<0.05$), and blood and fresh frozen plasma (FFP) transfusion volume ($p<0.05$ for both) were higher in group 2. The length of intensive care unit stay was longer in patients with comorbid coronary artery disease ($p<0.05$), bleeding, cardiac tamponade ($p<0.005$), prolonged ventilation ($p<0.001$), and those on inotropic support ($p<0.001$). Logistic regression analysis of the variables with significant differences between the two groups revealed that the blood transfusion was an independent predictor for long-term survival (OR 1.33, 95% CI; 1.02-1.74, $p=0.035$). The probability of actuarial survival was found to be 98%, 94.8% and 93.5% at one, five and ten years, respectively.

Conclusion: Prolonged length of intensive care stay along with associated risk factors may affect the long-term survival of the patients operated using the ASCP technique. These risk factors should be established and controlled, while vascular risk factors should also be considered to achieve a long-term survival.

Key words: Aortic aneurysm; dissecting aneurysm; follow-up studies; morbidity; mortality.

Amaç: Bu çalışmada antegrad selektif serebral perfüzyon (ASSP) tekniği ile kliniğimizde ameliyat edilen çıkan ve arkus aort anevrizma tamiri veya aort diseksiyonu yapılan hastalarda uzun dönem sağkalımı etkileyen faktörler araştırıldı.

Çalışma planı: Ocak 2000 - Aralık 2008 tarihleri arasında, ASSP tekniği ile kliniğimizde ameliyat edilen 177 hastadan sağ kalan ve hastaneden taburcu edilmiş olan 154 hasta (89 erkek, 65 kadın; ort. yaş 54.5±12.4 yıl; dağılım 20 - 84 yıl) çalışmaya dahil edildi. Seksen dört hastaya (%54.5) diseksiyon ameliyatı ve 70 hastaya (%45.5) anevrizma tamiri yapıldı. Takip sürecinde sağ kalan hastalar grup 1'de, kaybedilen hastalar ise grup 2'de yer aldı.

Bulgular: Ortalama takip süresi 50.5±26.8 (dağılım 3-106) ay idi. Takip sürecinde 10 hasta kaybedildi. Mortalite oranı %6.49 idi. Yoğun bakım kalış süresi ($p<0.05$) ve kan ve taze donmuş plazma (TDP) transfüzyon hacmi ($p<0.05$ her ikisi için) grup 2'de yüksek idi. Yoğun bakım kalış süresi eşlik eden koroner arter hastalığı ($p<0.05$), kanama ($p<0.005$) kardiyak tamponad ($p<0.005$), uzamış ventilasyon ($p<0.001$) ve inotropik destek gereksinimi olan hastalarda ($p<0.001$) daha uzundu. İki grup arasında anlamlı farklılık gösteren değişkenler ile yapılan lojistik regresyon analizinde ise, kan transfüzyonunun uzun dönem sağkalım için bağımsız bir öngördürücü olduğu saptandı (OR 1.33, %95 CI; 1.02-1.74, $p=0.035$). Bir, beş ve on yıllık aktüeryal sağkalım sırasıyla %98, %94.8 ve %93.5 olarak bulundu.

Sonuç: Uzamış yoğun bakım kalış süresi ve ilişkili risk faktörleri, ASSP tekniği kullanılarak ameliyat edilen hastaların uzun dönem sağkalımlarını etkileyebilir. Uzun süreli sağkalım elde etmek için, bu risk faktörlerinin belirlenmesi ve kontrolü ile birlikte vasküler risk faktörleri de göz önünde bulundurulmalıdır.

Anahtar sözcükler: Aort anevrizması; disekan anevrizma; takip çalışmaları; morbidite; mortalite.

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Correspondence: Anıl Özen, M.D. Türkiye Yüksek İhtisas Eğitim ve Araştırma Hastanesi Kalp ve Damar Cerrahisi Kliniği, 06230 Sıhhiye, Ankara, Turkey.
Tel: +90 533 - 736 43 43 e-mail: ozenanil@hotmail.com

Patients diagnosed with an aortic aneurysm and/or aortic dissection possess comorbidities such as hypertension (HT), chronic obstructive pulmonary disease (COPD), chronic renal failure, and heart failure and these combine with multiple organ ischemia and increased blood and blood product usage during surgery to become the primary factors which contribute to surgical morbidity and mortality. However, technological advances and an improved understanding of cardiopulmonary pathophysiology have resulted in safer repair and replacement of the segments of the thoracic aorta.

Protecting the brain, spinal cord, heart, and other vital organs is crucial during these long complex operations. In addition, it is important to keep the part of the aorta in question between the clamps or stop the circulation completely in order to perform the surgery in a blood-free environment. Although deep hypothermic circulatory arrest and retrograde cerebral perfusion[1,2] were preferred in the past, an increasing number of surgeons have recently started documenting their experiences with the antegrade perfusion technique.[3-8]

Since 1996, we have been using antegrade selective cerebral perfusion (ASCP) via right brachial artery cannulation on patients diagnosed with ascending and arcus aorta aneurysms and/or dissections of the aorta. Most of the published studies have focused on the safety of ACSP, Therefore, in this study, we focused on the factors that influence long-term survival via the use of the ASCP technique in surgery involving the thoracic aorta.

PATIENTS AND METHODS

From January 2000 to December 2008, 177 patients were operated on in our hospital using the ASCP technique, and the in-hospital mortality rate was 12.9% (n=23). The remaining 154 (89 male 65 females; mean age 54.5±12.4 years; range 20 to 84 years), were included in this retrospective study, and their informed consent was obtained prior to surgery. All were assessed via outpatient clinic visits or by telephone conversations (18.9%, n=29), and the factors affecting their postoperative long-term survival were then evaluated.

All of the patients had been diagnosed with an aortic aneurysm and/or aortic dissection. During the follow-up period (mean 50.6±26.9 months; range 3-106 months), 10 (6.49%) of the 154 study participants died. The remaining 144 patients were placed in group 1 while the 10 who did not survive were placed in group 2. The following information was obtained and analyzed for both groups and is shown in Table 1: gender, age, diameter of the aneurysm, time to discharge, cross-clamp duration, cardiopulmonary bypass (CPB), ASCP, cooling temperatures, type of operation, time in the intensive care unit (ICU), drainage, ventilation period, inotropic support, number

Table 1. Demographic data of the patients (n=154)

	n	%	Mean±SD	Range
Gender				
Male	89	57.8		
Female	65	42.2		
Age (years)			54.5±12.4	20-82
Hypertension	75	70.8		
Chronic obstructive pulmonary disease	38	24.7		
Diabetes mellitus	25	23.6		
Obesity	15	14.2		
Number of smokers	35	33.0		
Previous cardiac surgery	41	26.6		
Conary artery bypass graft	29	70.7		
Valve	12	29.3		
Coronary angiography (n=63)				
Coronary artery disease (+)	29	46.0		
Coronary artery disease (–)	34	54.0		
Diagnosis (n=154)				
Type 1 dissection	71	46.1		
Type 2 dissection	13	8.4		
Aneurysm	70	45.5		

SD: Standard deviation.

of blood and fresh frozen plasma (FFP) transfusions, smoking history, obesity, diabetes mellitus (DM), HT, family medical history, diagnosis, rupture, coronary artery disease (CAD), previous cardiac surgery, neurological complications, hemorrhage, tamponade, treacheostomy, medical emergencies, and arrhythmias. We then investigated the factors that influenced the long-term survival of the patients.

Operative technique

The surgical technique used was explained in detail in our previously published articles.[8] The patient lies in the supine position with the right arm externally rotated and abducted to 90 degrees. The arterial cannula is then inserted into the upper part of the right brachial artery distal to the axillary fossa. Following a median sternotomy, a two-staged venous cannula is placed into the right atrium, and CPB is initiated. Thereafter, the cross-clamp is applied, and cardiac arrest is achieved as cardioplegia is administered via the antegrade and the retrograde (via the coronary sinus) routes. According to the pathology of the patient, the proximal anastomosis is completed, and the patient is cooled down to 26-28 °C (measured by a rectal temperature probe). In addition, the outflow is decreased to about 8-10 ml/kg/min. Meanwhile, vascular clamps are placed on the innominate artery, left carotid artery, and subclavian artery, and the cross-clamp on the ascending aorta is removed. During this time, the cerebral blood flow is supplied by the right carotid artery via the right brachial artery. All of the arcus aorta reconstructions and anastomoses are performed using the open distal anastomosis technique during which the low output antegrade cerebral perfusion is continued via the right brachial artery. The types of operations performed on the participants in this study are presented at Table 2.

Table 2. Types of operations performed

	Group 1 (n=144)	Group 2 (n=10)
Supracoronary graft	76	1
Valved conduit	1	1
Modified Bentall procedure	11	2
Hemi-arcus replacement	4	1
Total arcus replacement	9	1
Cabrol procedure	1	-
Tirone David aortic root replacement	2	-
Magdi Yacoub procedure	3	1
Bentall + Hemi-arcus	9	1
Supracoronary + Hemi-arcus	28	2

Statistical method

Statistical analysis was performed using the SPSS version 16.0 for Windows software program (SPSS Inc., Chicago, Il, USA), and a p value of ≤0.05 was accepted as being statistically significant. Prior to the analyses, we sought to make sure that the data agreed with a certain number of hypotheses so we used the Kolmogorov-Smirnov test to analyze the data with regard to normal distribution, and Levene's test to test the coherence of the homogenous variance hypothesis. In addition, the Mann-Whitney U test was used to compare the average age, aneurysm diameter, ejection fraction (EF), follow-up period, time to discharge, cross-clamp duration, CPB duration, ASCP duration, cooling temperature, type of operation, length of time in ICU, drainage, ventilation period, inotropic support, blood transfusion, and FFP transfusion between the patients in groups 1 and 2. Furthermore, to analyze the factors that affected the patients' long-term survival, the Kaplan-Meier curve and log-rank analysis were used, and the odds ratios (ORs) and 95% confidence intervals (CIs) were estimated using a logistic regression model that was created to determine the independent predictors of long-term mortality.

RESULTS

The data regarding the long-term survival of the patients (excluding in-hospital mortality) is shown in Figure 1, and this revealed that the probability of actuarial survival was 98%, 94.8% and 93.5% at one, five, and 10 years, respectively. One patient who underwent concomitant

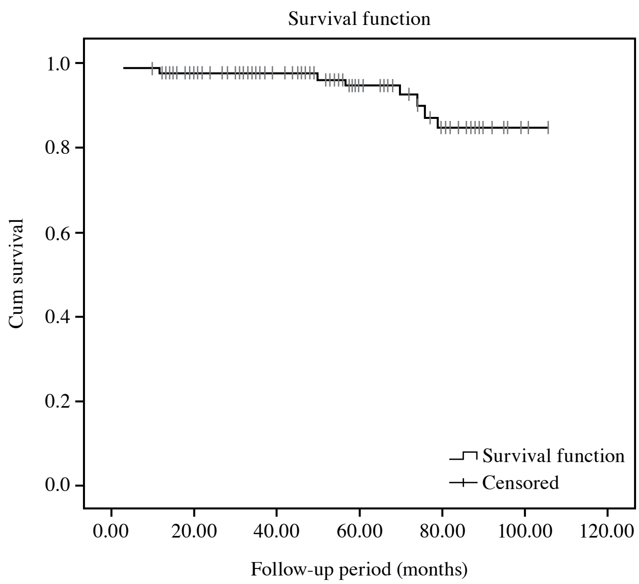

Figure 1. The probability of long-term survival of the patients (excluding in-hospital mortality) was 98%, 94.8%, 93.5% at 1, 5 and 10 years respectively.

Table 3. Outcomes and deaths occurring during the follow-up period

Outcomes	Number of patient
First year	
Atrial fibrillation	1
Hemiparesis	1
Numbness of the right arm	7
Between 1 and 5 years	
Endocarditis (aortic valve)	1
Vertigo	1
Pneumonia	1
Pericardial effusion	1
After 5 years	
Amnesia	1
Alzheimer's disease	1
Cause of death	10
First year	3
Neurological complications	2
Sudden death	1
Between 1 and 5 years	5
Pneumonia	1
Sudden death	2
Acute renal failure	1
Myocardial infarction	1
After 5 years	2
Sudden death	1
Myocardial infarction	1

valvular surgery sustained a left-sided hemiparesis at the 36th postoperative month which resolved three months later, and another developed a pericardial effusion secondary to uremia at the 49th postoperative month. Additionally, echocardiography detected a first-degree perivalvular leak secondary to endocarditis of the aortic valve in one patient, and biannual echocardiographic follow-up was recommended. In group 2, two of the patients were over the age of 60 and had no short-term postoperative neurological complications. However, they died from cerebrovascular accidents (CVAs) at the third and 12th postoperative months respectively. Two of the patients in this group died following a myocardial infarction (MI). Both of them had a history of coronary artery bypass graft (CABG) surgery and were found to have patent grafts and EFs ranging from 35-40% prior to surgery. The data regarding the outcomes and deaths which occurred during the follow-up period are provided in Table 3.

A comparison of the factors that influenced the long-term mortality in groups 1 and 2 is also shown in Table 4 along with the effects of the operative and postoperative measures on the patients' long-term survival. Longer ASCP duration had no effect, but our analysis revealed that the time in ICU along with the number of blood and FFP transfusions were significantly higher in the patients with long-term mortality. In addition, other factors, such as the presence of CAD (p=0.043), re-exploration due to bleeding (p=0.000) or tamponade (p=0.004), prolonged ventilation (p=0.000), and inotropic support (p=0.000) were analyzed for an additional five days or more and were then accepted as being responsible for a prolonged length of time in the ICU.

The parameters between the two groups that were deemed to be significant also underwent further analysis via a logistic regression model, and the only independent predictor for long-term mortality was the number of blood transfusions (OR 1.33; 95% CI 1.02-1.74; p=0.035).

DISCUSSION

The search for more effective techniques that can provide longer protection periods during aortic surgery has been fruitful, and these have been put into practice. More recently, ASCP has been used for cerebral protection during aortic dissection and aneurysm

Table 4. Comparison of the intraoperative and postoperative data related to long-term survival

	Group 1 (n=144) Mean±SD	Group 2 (n=10) Mean±SD	*p*
Discharge period (days)	11±10.8	17.1±18.2	0.282
Cross-clamp duration (minutes)	90.2±33.7	102.3±26.4	0.146
Cardiopulmonary bypass duration (minutes)	142.5±53.6	154.6±33.3	0.260
Antegrade selective cerebral perfusion duration (minutes)	27.4±14.1	18.4±9.0	0.016*
Intensive care unit stay (days)	3.6±6.9	11.3±18.8	0.037*
Drainage (ml)	756.0±542.9	575.0±309.5	0.267
Ventilation duration (hours)	41.6±141.1	48.4±69.5	0.224
Inotropic support (hours)	71.7±128.7	103.3±89.8	0.103
Blood transfusions (units)	2.6±3.0	7.3±8.7	0.008*
Fresh frozen plasma transfusions (units)	3.8±5.2	8.7±11.6	0.013*

SD: Standard deviation; * Statistically significant.

operations, and Bachet et al.[3] and Kazui et al.,[4] whose studies featured largest series, defended this technique because it provides more time for longer repairs.

In our hospital, we have been using ASCP for cerebral protection during aortic dissection and aneurysm operations since 1996. In light of our previous studies and anatomical knowledge, it is evident that the blood flow to the contralateral side during unilateral ASCP is sufficient.[8-10] To our knowledge, not much data has been published concerning long-term survival following aortic surgery with ASCP; hence we focused on this topic and determined that the survival rate was 93.5% at 10 years, which was a positive outcome of our retrospective study.

Postoperative follow-up of these patients is essential since there are numerous factors which can affect early and late postsurgical mortality. Our study revealed that prolonged ICU stays affect long-term mortality. Furthermore, patients with CAD, those requiring inotropic or prolonged ventilatory support, and those who have undergone re-exploration due to tamponade and/or bleeding spent more time in the ICU. Uchida et al.[11] similarly found that pulmonary disease and postoperative bleeding affects long-term survival while Kirsch et al.[12] also declared that previous pulmonary disease had the same outcome. Furthermore, in a study by Lei et al.,[13] made up of 298 patients who underwent arcus aorta surgery, they investigated the pre- and intraoperative factors that influenced prolonged ICU admission postoperatively and found that inotropic support was the main culprit, as we also discovered in our research. The predominant cause of mortality among patients undergoing thoracic aortic surgery during follow-up is vascular in origin.[11,14] In our study, 10 patients died during the follow-up period, and vascular complications, MI, sudden death, or cerebrovascular accidents were responsible for eight of them.

Once the factors affecting ICU duration have been determined, specific management strategies can be devised for patients at an increased risk in order to reduce the time spent there. Those who have had long stays in the ICU should be followed up while also keeping in mind the contributing factors. Since death due to vascular causes during long-term follow-up is predominant, appropriate management of vascular risk factors (diabetes, hypertension and hyperlipidemia) is essential. Done properly, this will have a positive effect on the long-term survival.

In our study, excess blood transfusions, perhaps as the result of prolonged ICU stays, were an independent predictor of long-term survival. However, the extended time in the ICU might also be caused by preoperative morbidities other than the type of surgery. However, in the logistic regression models that included all of the preoperative demographic variables, we identified no preoperative variables that influenced our patients' long-term survival. As the number of deceased patients was relatively low in our study, these analyses are subject to misinterpretation.

In addition, this study was a retrospective, single-center study, having different surgical teams perform the operations might be seen as a limitation. Although the surgical technique was performed in exactly the same manner, the surgical experience of the teams varied. In addition, 18.9% (n=29) of the patients could not be examined in person due to their distance from the hospital and had to be interviewed over the telephone. While this did not affect the identification of postoperative long-term mortality, the lack of face-to-face interviews and in-person examinations most likely limited our ability to gather adequate information.

Conclusion

We found that prolonged stays in the ICU and the factors associated with this along with the amount of transfused blood products were all related to the long-term survival of patients who underwent surgery using the ASCP technique. These factors need to be identified and managed, and the patients should be followed up closely to ensure a positive effect.

Declaration of conflicting interests

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