

Open Heart Surgery Applications in Dogs Suffering from Natural Infection of *Dirofilaria immitis**

Zülfikar Kadir SARITAŞ

Department of Surgery, Faculty of Veterinary Medicine, Afyon Kocatepe University, Afyon – TURKEY
e-mail: zksaritas@hotmail.com

Faruk AKIN

Department of Surgery, Faculty of Veterinary Medicine, Ankara University, Ankara - TURKEY

Mehmet ŞAHAL

Department of Internal Medicine, Faculty of Veterinary Medicine, Ankara University, Ankara - TURKEY

Naci ÖCAL

Department of Internal Medicine, Faculty of Veterinary Medicine, Kırıkkale University, Kırıkkale - TURKEY

Received: 23.07.2003

Abstract: This study includes 6 dogs naturally infected with *Dirofilaria immitis* of different ages and sexes.

Clinical, radiographical, blood gas and blood biochemical evaluations were examined in the preoperative period. Microfilariae were determined in 6 cases with a modified Knott test. Cardiopulmonary bypass (CPB) and open-heart surgery were carried out.

Animals were prepared for cannulation under general anesthesia. The heart was approached by right lateral thoracotomy. The femoral artery and vena cava were cannulated before CPB. During the operation, arterial blood pressure and the heart rate were monitored and blood gas values were continuously observed. Before and 1 hour after the operation cardiac output was monitored. Mean operation time was 155 ± 35 minutes, and cross-clamp time was 34 ± 9 minutes. A total of 12 ± 5 mature *Dirofilaria immitis* were collected from the right heart and the pulmonary artery.

Radiographical evaluation showed that the heart was hypertrophic in all cases and right heart dilatation was seen in one case. In blood gas analysis, an increase in pCO_2 and decreases in pO_2 , HCO_3 and pH were observed.

One dog was extubated for 1 hour, while the remaining 5 dogs were extubated for 3 hours after the operation. One dog was followed for 1.5 years whereas the others were followed for 6 months after surgery.

No complications occurred during the operation, but premature ventricular contractions were observed in all cases. Arterial blood pressure and cardiac output decreased significantly when compared to preoperative values 1 hour after the operation. The heart rate increased significantly. In two cases, a postoperative superficial infection was identified.

Two dogs were still infected with microfilariae two weeks after the operation. Ivermectin was administered and the microfilariae were destroyed two months after this medication.

All dogs tolerated the CPB and open-heart surgery procedures well.

Key Words: *Dirofilaria immitis*, cardiopulmonary bypass, dog

***Dirofilaria immitis* ile Doğal Enfekte Köpeklerde Açık Kalp Cerrahisi Uygulamaları**

Özet: Araştırmanın materyalini *Dirofilaria immitis* ile doğal olarak enfekte olmuş 6 adet değişik yaş ve cinsiyette köpek oluşturmuştur. Olgularda preoperatif dönemde klinik, radyografik, kan gazları ve kan biyokimya analizleri gerçekleştirilmiştir. Yapılan modifiye Knott testinde mikrofililer saptanan 6 olguda kardiyopulmoner baypas (KPB) ve açık kalp cerrahisi gerçekleştirilmiştir.

Preoperatif radyografik incelemede tüm olgularda kalpte büyüme bir olguda ileri sağ kalp dilatasyonu belirlenmiştir. Kan gazları analizinde pCO_2 'de yükselme kaydedilirken; pO_2 , HCO_3 ve pH'da düşüş kaydedilmiştir.

Genel anestezi altında olgularda kanülasyon için gerekli hazırlık gerçekleştirilmiş, sağ lateral torakotomiyle kalbe ulaşılmış ve A. femoralis ile vena kava'lar KPB için kanüle edilmiştir. Olgularda operasyon boyunca arteriyel kan basıncı, dakika kalp frekansı monitörize edilmiş ve kan gazları sürekli olarak izlenmiştir. Operasyon öncesi ve operasyondan 1 saat sonra kardiyak debi

* This research was performed at the University of Ankara, Faculty of Veterinary Medicine, Department of Surgery, Experimental Surgery Research Unit, and was supported by TÜBİTAK (Project No: DECAR-1).

monitörizasyonu gerçekleştirilmiştir. Toplam operasyon süresi 155 ± 35 dakika, kros klemp süresi 34 ± 9 dakika olarak belirlenmiştir. Olgulardan 12 ± 5 adet olgun *Dirofilaria immitis* sağ kalpten ve A. pulmonaristen uzaklaştırılmıştır.

Olgulardan biri postoperatif 1. saatte, diğer 5 olgu ise 3. saatte ekstübe edilmiştir. Bir olgu 1,5 yıl diğer olgular 6 ay süre ile kontrol edilmiştir.

İntraoperatif önemli bir komplikasyona rastlanmazken, postoperatif olguların tümünde prematüre ventriküler kontraksiyon gelişmiştir. Postoperatif 1. saatte arteriyel kan basıncında ve kardiyak debide preoperatif değerlere göre istatistiksel önemi olan bir düşüş saptanmıştır. Buna karşın dakika kalp frekansı ise anlamlı bir şekilde artmıştır. İki olguda postoperatif derialtı yüzlek enfeksiyon izlenmiştir.

Postoperatif 2. haftada 2 olguda mikrofililerin varolduğu, ivermektin uygulamasından sonra 2. ayda mikroflerlere rastlanmadığı gözlenmiştir.

Olguların tümü KPB (kardiyopulmoner bypas) ve açık kalp cerrahisi prosedürünü iyi tolere etmiştir.

Anahtar Sözcükler: *Dirofilaria immitis*, kardiyopulmoner baypas, köpek

Introduction

Dirofilaria immitis is a nematode. It is a frequently seen parasite in dogs and in other species such as cats, foxes, bears, wolves, and horses and rarely in humans (1-6).

The mature form of the parasite lives in the right ventricle of the heart or in the pulmonary artery (1,3,4,6,7). The female forms release several thousand larvae into the blood (1,4,6,8).

Environmental factors like temperature, mosquitoes, and aging play an important role in *D. immitis* infection in dogs (9).

The infection risk increases at the age of 4-7 years. Male dogs carry a higher risk almost twice as much as females of succumbing to such parasites (1,10-12). Elderly dogs, those 8 or 9 years old, have a decreased risk of infection although this may be because most deaths occur by this age. In addition the immune system prevents the maturation of the parasites in this age group (1,10).

Infected dogs sometimes do not show any clinical signs. The initial signs of infection are restricted movements and weight loss followed by coughing, respiratory difficulties and chest pains (1,2,4,13-15). Pulmonary edema, right heart insufficiency and ascites worsen the clinical situation (1,13,14). Following severe and long-lasting infections, pulmonary vascular disorders occur and end in pulmonary hypertension. In addition, intimal hyperplasia, thromboembolic events, arterial wall injury and parenchymal lesions are all associated with pulmonary hypertension (1,13,15-17).

The increased vascular resistance leads to acute right heart failure (1,13). Pulmonary hypertension was the main cause of the symptoms in the infected dogs. Heart murmurs can be heard along with signs of hypertension and ascites (1,17). The massive presence of live parasites in the pulmonary artery prevent blood flow and increase blood pressure (1,13,17).

Imbalanced blood gases, increased hepatic enzyme levels, loss of liver functions, proteinuria and uremia can be seen in dirofilariasis with pulmonary, cardiac and hepatic disorders. In severe cases, the pO_2 level is 40.0 mmHg, although healthy subjects have 55.3 mmHg (1,18).

In physical examination, the paradoxical second heart sound due to the delay of the evacuation of the right ventricle, a harsh respiration sound and laboratory tests, such as leukocytosis and the existence of microfilariae in the blood can be observed for diagnosis (1,19). Immunological tests are very accurate for diagnosis. Right heart and pulmonary artery dilatation is related to pulmonary hypertension (1,20). The degree of the illness can be determined by using two-dimensional echocardiography (1,21).

There are medical and surgical treatment methods for *Dirofilaria immitis*. The most radical method for the treatment of mature forms is surgery. Jugular venotomy (21-25), pulmonary arteriotomy (26-28), removal of parasites from the right ventricle (28), inflow occlusion and right ventriculotomy (28) and extracorporeal circulation (29) are among the surgical methods available.

The initial use of open-heart surgery for *D. immitis* infection in 6 dogs in Turkey is reported in this paper.

Materials and Methods

Six dogs of different ages, breeds and sexes were used in the study. The mean weight of the animals was 28 ± 5 kg. The study was carried out in accordance with the 'Principles of Laboratory Animal Care' and 'Guide for the Care and Use of Laboratory Animals' (NIH Publication No.80-23, revised 1985) following the approval of our ethics committee.

The dogs were first admitted to the internal medicine department. The clinical examination and modified Knott test confirmed the diagnosis as *D. immitis* infection, and the dogs were referred to the surgery department.

Preoperative Preparation

The animals were not allowed to eat 24 hours before surgery. If they had ascites or pericardial tamponade, they were drained before surgery. Cefazolin sodium (20 mg/kg) was infused intravenously 12 hours before and again just before the operation.

Anesthesia Protocol

An 18 G catheter was placed in the vena cephalica antebrachii and 10 ml/kg per hour of ringer lactate solution was given before the operation. The left lateral side of the thorax and left femoral regions were clipped and disinfected before surgery. Premedication was made with atropin sulfate (0.04 mg/kg, subcutaneous injection) 45 min prior to surgery. The animals were sedated with xylazine HCl (2 mg/kg i.m.) 30 min. after premedication. To induce anesthesia, a combination of fentanyl citrate (5 mcg/kg), thiopental sodium (15 mg/kg) and atracurium (90 mcg/kg) were given intravenously. Once respiratory depression was observed, the animals were intubated. The dogs were ventilated with 40% of FiO_2 and 15 ml/kg per min tidal volume 16 times per minute. Anesthesia was maintained by bolus doses of thiopental sodium.

The operation side was prepared for aseptic surgery. The left femoral artery and venae were catheterized. An arterial line was used for blood pressure measurements and blood gas analyses and was connected to the monitor with a transducer. Electrocardiography (ECG) electrodes were also placed on the extremities and ECG was monitored. Blood pressure was continuously monitored with the multichannel monitor. A swan-ganz thermodilution catheter was placed in the pulmonary artery via the femoral venae for cardiac output monitoring as reported by Saritaş et al. (30).

Cardiopulmonary Bypass (CPB) Procedure

Prime solution

A 1.5-l ringer lactate solution, 44 mEq sodium bicarbonate and a 1 ml/kg, 20% mannitol solution were used for the initiation of the circulation in CPB. 5000 IU heparin was added for anticoagulation and ACT was held above 480 s.

Thoracotomy and Cannulation

The fourth right intercostal space was used for the thoracotomy and the ribs were separated. Pericardiectomy was done carefully while protecting the phrenic nerves, and the pericardium was attached to the thorax with 3/0 silk sutures (Figure 1). The ascending aorta was prepared with purse string sutures (4/0 polypropylene (Prolen)) for the aortic catheterization. A right atrium was used for venous cannulation with 2/0 vicryl sutures. Heparin (300 U/kg) and a total dose of 250 mg methylprednisolon (Prednol) were infused before cannulation.

Cannulation

The arteria femoralis was used for arterial cannulation and an 18 Fr arterial cannula was used. Two venous cannulas were inserted into the vena cava caudalis and cranialis via the right ventricle. A 12 G infusion cannula was inserted into the ascending aorta for cardioplegic infusion with the Y-shaped connection for air evacuation before declamping (Figure 2).

Cardioplegic Solution Application

A + 4 °C crystalloid cardioplegic solution was used to stop the heart in order to protect it during the ischemic period. The solution contained 27 m Eq Na^+ , 30 m Eq K^+ , 57 m Eq Cl^- , 6 m Eq Mg^{++} , 6 m Eq SO_4 , 4 m Eq Tromethamine and 50 g Dextrose monohydrate (31).

Cardiopulmonary Bypass

A Debaquey pump and membrane oxygenator were used for the CPB. Arterial and venous connections were made with the pump. The flow was adjusted to 2.5 l/m² per minute and was increased until the arterial blood pressure exceeded 60 mmHg. All of the dogs were cooled down to 28 °C rectal temperature.

Cardiac Arrest

After placing the cross-clamp on the aorta, 1 l cold (+4 °C) crystalloid cardioplegic solution (St. Thomas) was infused for rapid cardiac arrest.



Figure 1. View of the Heart after Pericardiectomy.



Figure 2. Cardiopulmonary Bypass Procedure and Cannulation.

Intracardiac Surgery

A right ventriculotomy was performed by creating a 4-6 cm incision from the lateral wall to the apex, and the exposure was obtained. Mature *Dirofilaria immitis* were visible both in the right ventricle and in the pulmonary artery. After removing the parasites from the heart, the ventricle was closed with double layer sutures. The first layer was simple and interrupted sutures, the second one

was continuous with 3/0 prolene sutures. The last suture was completed by compressing the right ventricle. Then the aortic clamp was removed and the heart was defibrillated. The remaining air was aspirated.

Once the dog's body temperature heated up to the 37 °C, CPB was terminated. The necessary positive inotropic agent dobutamine was started to bring the systemic blood pressure above 80 mmHg, the cannulas were taken

out, 7/0 and 4/0 prolene were used to repair the arterio femoralis and the right atrium. The blood that remained in the reservoir was placed in plastic bags and infused. Acid-base disturbances were balanced by infusing bicarbonate solutions. The heparin that was initially infused was reversed with protamine sulfate (4.5 mg/kg) (32). A normal heart rhythm was maintained by using arrhythmic infusion. The dogs were defibrillated when ventricular fibrillation occurred.

Thorax Closure

Hemostasis was corrected by either cauter coagulation or ligatures. A 32 Fr thorax drain was located after the closure. The ribs were closed by three separate sutures. Muscles, above the ribs, were closed with 0/0 vicryl. Skin was closed with interrupted sutures using 2/0 prolene. Thorax drainage was continued until satisfactory intrathoracic pressure and hemorrhage were achieved. Positive pressure ventilation was used during this period.

Postoperative care

In the postoperative period, positive pressure ventilation was continued until the drain was removed. Mepheridin hydrochloride (25-50 mg iv) and morphine sulfate (10 mg iv) were administered for sedation and postoperative pain management.

Statistical Analysis

All values were presented as the mean \pm standard deviation. The difference among the pre and postoperative values were determined by Student's t-test. The significance level was set at $P < 0.05$ (33).

Results

Preoperative Clinical Findings

Clinical examination of the infected dogs revealed a tricuspid valve murmur during auscultation. Five cases had respiratory distress and exercise intolerance. Two cases had severe ascites and one had cachexia.

Hematological Findings

The mean RBC, WBC, MCV, HCT and Hb values are shown in Table 1. RBC was found below the limit and WBC was significantly high (Table 1).

Blood Gas Analysis

Preoperative blood gas analysis results were presented as mean \pm standard deviation and shown in

Table 2; pH values were found at the lower border, PCO_2 was above the reference values, and PO_2 was low. HCO_3 level and base excess values were also low (Table 2).

Radiological Findings

Two-way radiographical investigation revealed that 4 cases had heart dilatation of different sizes and one of them had severe dilatation (Figure 3).

Intraoperative Findings

The total operation duration was 155 ± 35 min and cross-clamp time was 34 ± 9 min. All dogs tolerated the operation well. One dog had severe heart dilatation, parallel to the preoperative findings as shown in picture 1. The mean of 12 ± 5 piece of mature forms of *Dirofilaria immitis* (Figure 4) were extracted from the right ventricle and pulmonary artery of each case.

Postoperative Findings

One of the cases was extubated one hour after surgery and the others were extubated three hours after surgery. All dogs had premature ventricular extrasystole, which was balanced by using lidocaine hydrochloride.

Table 1. Blood profile in Dogs with Dirofilariosis.

Parameter	Normal Value	Obtained Value Mean \pm Standard Deviation
RBC ($10^6/mm^3$)	5.5-8.5	5.62 ± 1.28
MCV (m)	60-77	65.5 ± 12.31
HCT (%)	37-55	40.17 ± 10.78
WBC ($10^3/mm^3$)	6-17	19.72 ± 2.64
Hb (g/dl)	12-18	2.55 ± 2.61

Table 2. Preoperative blood gas analyses in dog with Dirofilariosis.

Parameter	Normal Value	Obtained Value Mean \pm Standard Deviation
PH (-log H ⁺)	7.31-7.42	7.318 ± 0.03
PCO_2 (mm Hg)	29-42	48.3 ± 4.32
PO_2 (mm Hg)	80-100	55 ± 4.69
HCO_3 (mmol/l)	20-25	$18.93 \pm 1.16 O_2$
Sat (%)	80-100	72.17 ± 0.47
BD (mmol/l)	-4,.0	-7.4 ± 2.78

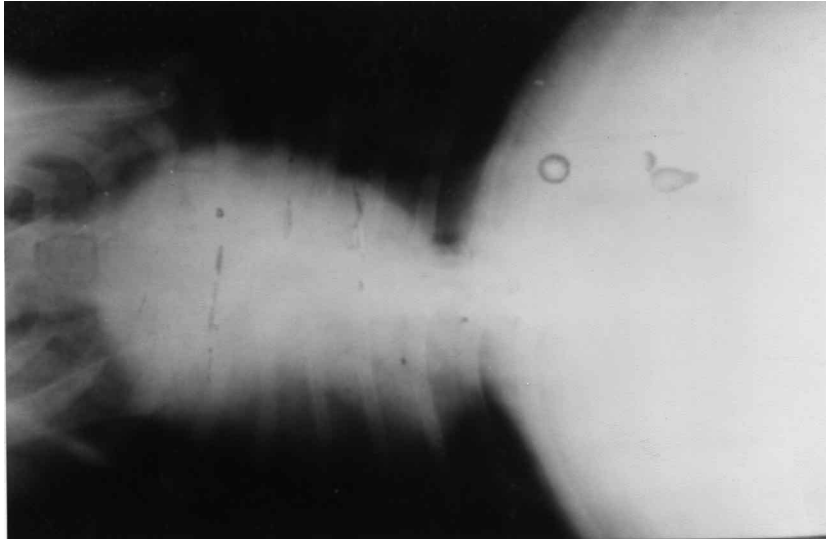


Figure 3. Radiographic appearance of the heart dilatation (case no: 4).



Figure 4. Removal of Mature Form of *Dirofilaria immitis* from the Right Heart.

The mean arterial blood pressure, cardiac output and heart rate values were statistically different at the first postoperative hour according to preoperative values. The preoperative and first postoperative mean arterial blood pressure values were 95 ± 8 mmHg and 75 ± 7 mmHg respectively ($P < 0.002$). Cardiac output was measured at 3.3 ± 0.48 l/min preoperatively and decreased to 2.25 ± 0.48 l/min postoperatively after the first hour ($P < 0.01$). The heart rate also increased from 133 ± 12 / min to 163 ± 9 / min at the postoperative first hour ($P < 0.002$).

One dog had emphysema at the incision side of the thorax 9 days after the operation. The dog was operated on again and the incision line was sutured. Two dogs had superficial infections on the thorax incision line and one had an infection on the femoral incision line. All dogs were treated with a suitable antibiotic, and drainage was applied.

Two dogs still had microfilariae in their blood. All cases were treated with ivermectin on the 15th postoperative day and the ivermectin treatment was

repeated one month later. Two dogs were treated for anemia and they completely recovered within two months.

Five cases had 6-month follow-up control and one dog had an 18-month follow-up control. All dogs had negative Knott tests in the 6th month. One dog had a thoracic incision and an anterior extremity infection in the 7th month and was treated with a systemic antibiotic treatment.

Discussion

Observing clinical symptoms of *D. immitis* in dogs not difficult. Reluctancy in movement, weight loss, coughing, respiratory difficulties and chest pains are the signs of infected dogs (1,2,4,13-15). Heart murmurs, ascites and hypertension can also be seen during this period (1,17). All of our cases had a tricuspid valve murmur, while five had respiratory difficulties and intolerance toward exercise. These were similar to the literature (1,17). Pulmonary edema, right heart insufficiency and ascites adversely affected the cases and worsened the clinical situation in the dogs infected with dirofilariasis (1,13,14). Two of our dogs had severe ascites and one had severe right heart dilatation. Although five of the cases had respiratory difficulties and right heart dilatation was observed in the radiographic evaluation, they did not have clinical findings because of this situation.

The vena cava caudalis can sometimes be obstructed acutely with *D. immitis* and this is called caval syndrome. The dogs had anemia, hemoglobinemia and hemoglobinuria (1,13,14,21,34). None of our cases had caval syndrome, but RBC and Hb levels were below limits in preoperative evaluation. Right heart insufficiency could be observed due to the increase in vascular resistance and one of our cases had right heart dilatation (1,13).

Most of the infected dogs developed pulmonary hypertension and the clinical symptoms were observed. The massive presence of live parasites in the pulmonary artery prevents blood flow in turn increasing blood pressure (1,13,17). In our cases, although arterial blood pressure was high, it cannot be identified as arterial

hypertension, indicating that parasites had not yet occluded the artery.

Blood gases were imbalanced when the dogs were severely affected. Although healthy dogs have 55.3 mmHg pO₂, the dogs in the study had 40.0 mmHg pO₂ in their venous blood (1,18).

In the study, the pH was low, the pCO₂ level was high and pO₂ was low in the blood gases during preoperative evaluation. In addition to these values, the HCO₃ level was low. The results were similar to the findings of Kitagawa et al. (18). These not only supported the intolerance towards exercise in the infected dogs, but also the collapse of respiration and circulation that developed during the infection.

The CPB can be effectively used in the dogs for several reasons such as the removal of cardiac parasites (31,35-37), the correction of ventricular and atrial septal defects (38), the correction of mitral valve repair (39) and experimental surgery.

Open-heart surgery and cardiopulmonary bypass affect homeostasis. It requires complex and advanced types of instruments and an educated staff. In humans, it is performed by using the ascending aorta for the arterial outflow and the right atrium for the venous inflow beside the median sternotomy. In dogs, lateral thoracotomy accompanies right atrial and femoral arterial cannulation (31).

In this study, surgery was carried out according to the literature and none of the cases had surgical complication during the cardiopulmonary bypass. In the postoperative evaluation, we did not have any complications due to coagulation or bleeding. We used membrane oxygenators and a non-hemic prime solution.

In this study, we did not experience any complications due to the open-heart procedure that was used for the first time in Turkey to treat dogs naturally infected with *D. immitis*. This surgical method can be safely used for treatment. In conclusion, cardiopulmonary bypass is a safe and successful approach for dogs and can be a treatment method for *D. immitis* infection but it is expensive and requires an educated staff.

References

1. Şahal, M., Özlem, M., Tanyel B., Öcal, N., Sel, T.: Köpeklerdeki dirofilariasis olgularında kan, idrar ve abdominal sıvıda biyokimyasal değişiklikler. Ankara Üniv. Vet. Fak. Derg., 1997; 44: 267-276.
2. Gutierrez, Y.: Diagnostic features of zoonotic filariae in tissue sections. Hum. Pathol., 1984; 15: 514-525.
3. Doğanay, A., Şahal, M.: Türkiye'de köpeklerdeki dirofilariasis sorunu ve insan sağlığı açısından önemi. Ankara Üniv. Vet. Fak. Derg., 1987; 34: 288-287.
4. Langer, H.E., Bialek, R., Mielke, H., Klose, J.: Human dirofilariasis with reactive arthritis-case report and review of the literature. Klin. Wochenschr., 1987; 65: 746-751.
5. Ro, J.Y., Tsakalaakis, P.J., White, V.A., Luna, M.A., Chang-Tung, E.G., Green, L., Cribbet, L., Ayala, A.G.: Pulmonary dirofilariasis: the great imitator of primary or metastatic lung tumor. Hum. Pathol., 1989; 20: 69-76.
6. Bailey, T.S., Sohrabi, A., Roberts, S.S: Pulmonary coin lesions caused By *Dirofilaria immitis*. J. Surg. Oncol., 1990; 44: 268-272.
7. Glickman, L.T., Grieve, R.B., Breitschwerdt, E.B., Mika-Grieve, M., Patronek, G.J., Domanski, L.M., Root, C.R., Malone, J.B.: Serologic pattern of canine heartworm (*Dirofilaria immitis*) infection. Am. J. Vet. Res., 1984; 45: 1178-1183.
8. Risher, W.H., Crocker, E.F.Jr., Becman, E.N., Blalock, J.B., Ochsner, J.L: Pulmonary dirofilariasis. J. Thorac. Cardiovasc. Surg., 1989; 97: 303-308.
9. Webster, M.C., Mcsporrnan, K.D., Pomroy, W.E.: No evidence of endemic infection with *Dirofilaria immitis* in dogs. New Zealand Vet. J., 1997; 45: 82.
10. Glickman, L.T., Grieve, R.B., Schantz, P.M.: Serologic pattern of zoonotic pulmonary dirofilariasis. Am. J. Med., 1986; 80: 161-164.
11. Rawlings, C.A.: Clinical laboratory evaluations of seven heartworm infected beagles: during disease development and following treatment. Cornell Vet., 1982; 72: 49-56.
12. Selby, L.A., Corvin, R.M., Hayes, H.M.: Risk factors associated with canine heartworm infection. J. Am. Vet. Med. Assoc., 1980; 176: 33-35.
13. Kitagawa, H., Sasaki, Y., Ishihara, K., Hirano, Y.: Contribution of live heartworms harboring in pulmonary arteries to pulmonary hypertension in dogs with dirofilariasis. Jpn. J. Vet. Sci., 1990; 52: 1211-1217.
14. Murdoch, D.B.: Heart worm in the United Kingdom. J. Small Anim. Pract., 1984; 25: 299-305.
15. Ravling, C.A., Calvert, C.A.: Heartworm Disease. In: Ettinger, S.J.: Textbook of Veterinary Internal Medicine. W.B. Saunders Comp. Philadelphia.,1989; 1163-1184.
16. Keith, J.C., Rawlings, C.A., Schaub, R.G.: Pulmonary thromboembolism during therapy of dirofilariasis with thiacetarsamide: modification with aspirin or prednisolone. Am. J. Vet. Res., 1983; 44: 1278-1283.
17. Sasaki, Y., Kitagawa, H., Hirano, Y.: Relationship between pulmonary arterial pressure and lesions in the pulmonary arteries and paranchyma, and cardiac valve in canine dirofilariasis. J. Vet. Med. Sci., 1992; 54: 739-744.
18. Kitagawa, H., Sasaki, Y., Ishihara, K., Kuwahara, Y.: Laboratory test results in artificial model of caval syndrome in canine heartworm disease. Jpn. J. Vet. Sci., 1993; 52:1123-1125.
19. Eyster, G.E., Gaber, C.E., Probst, M.: Cardiac Disorders. In Textbook of Small Animals Surgery. Ed: Slatter D. Chapter 58. Vol: I. W.B. Saunders Co. USA. 1993.
20. Jackson, R.F., Treatment of heartworm-infected dogs with chemical agents. J. Am. Vet. Med. Assoc., 1969; 154: 390-393.
21. Ishihara, K., Kitagawa, H., Sasaki Y.: Efficacy of heartworm removal in dogs with dirofilarial hemoglobinuria using flexible alligator forceps. Jpn. J. Vet. Sci., 1988; 50: 739-745.
22. Jackson, R.F., Seymour, W.G., Grovney, P.J., Otto, G.F.: Surgical treatment of the caval syndrome of canine heartworm disease. J. Am. Vet. Med. Assoc., 1977; 171: 1065-1069.
23. Howard, P.E., and Pitts, R.P.: Use of fiberoptic accessory for retrieval of adult hertworms in a dog with postcaval syndrome. J. Am. Vet. Med. Assoc., 1986; 189: 1343-1344.
24. Sasaki, Y., Kitagawa, H., Ishihara, K., Masegi, T.: Improvement in pulmonary artery lesion after heartworm removal using flexible alligator forceps. Jpn. J. Vet. Sci., 1990; 52:743-752.
25. Kitagawa, H., Sasaki, Y., Ishihara, K., Kawakami, M.: Cardiopulmonary function values before and after heartworm removal in dogs with caval syndrome. Am. J. Vet. Res., 1991; 52: 126-132.
26. Horne, R.D.: Evaluation of pulmonary arteriotomy for the removal of *Dirofilaria immitis*. J. Am. Vet. Med. Assoc., 1962; 141: 248-255.
27. Abadie, S.H., Black, E., Dupuy, H.J., Gonzales, R.: A procedure for the surgical removal of *Dirofilaria immitis*. J. Am. Vet. Med. Assoc., 1970; 156: 884-889.
28. Eyster, G.E.: Basic Cardiac Surgical Procedure. Ed: Slatter D. Chapter 60 Vol: I. W.B. Saunders Co. USA. 1993; 893-918
29. Holmberg, D.L.: Extracorporeal Circulatory Support. in Textbook of Small Animals Surgery. Ed: Slatter D. Chapter 61. Vol: I. W.B. Saunders Co. USA. 1993.
30. Sarıtaş, Z., Koç, B., Akın, F.: Köpeklerde balon tipi Sawm-Ganz termodilüsyon kateteri ile pulmoner arter (sağ kalp) kateterizasyonu. (108 Olgu). Vet. Cerrahi Derg., 1999; 5: 28-35.
31. Klement, P., Del Nido, P.J., Mickleborough, L., Mackay, C., Klement, G., Wilson, G.J.: Technique and postoperative management for successful cardiopulmonary bypass and open-heart surgery in dogs. J. Am. Vet. Med. Assoc., 1987; 190: 869-874.

32. Katircioğlu, S.F., Saritaş, Z., Ulus, A.T., Yamak, B., Yücel, D., Ayaz, S.: Iloprost added to the cardioplegic solutions improves myocardial performance. *Prostaglan. Lipid Mediator.*, 1998; 55: 51-65.
33. Düzgüneş, O., Kesici, T., Gürbüz, F.: İstatistik Metodları I. Ankara Üniv. Ziraat Fak. Yay. Ders Kitabı: AÜ Basımevi. Ankara. 1993.
34. Kitagawa, H., Sasaki, Y., Ishihara, K.: Clinical studies on canine dirofilarial hemoglobinuria: measured and calculated serum osmolarities and osmolar gap. *Jpn. J. Vet. Sci.*, 1989; 51: 703-710.
35. Shiang, H., Asirvatham, J., Lee, T.S., Silvay, G., Mitchell, B., Mathiesen, E., Szabo, T., Liu, S.K., Litwak, R.: Surgical removal of canine heartworms, using cardiopulmonary bypass. *J. Am. Vet. Med. Assoc.*, 1973; 163: 981-983.
36. Shiang, H., Jurado, R., Liu, S.K., Chen, V., Calem, J., Litwak, R.S.: Nine-month evaluation of dogs after open heart surgical removal of heartworm. *J. Am. Vet. Med. Assoc.*, 1987; 190: 1425-1426.
37. Rohn, D.A., Davis, K.L., Mehlhorn, U., Allen, S.J., Laina, G.A.: Myocardial edema and compromised left ventricular function attributable to dirofilariosis and cardiopulmonary bypass in dogs. *Am. J. Vet. Res.*, 1995; 56: 221-223.
38. Eyster, G.E., Anderson, L.K., Krehbeil, J.D., Whipple, R.D., Blanchard, G.L., Dickason, J., Braden, T.D., Bohonowych, R., Harris, F.: Surgical repair of atrial septal defect in a dog. *J. Am. Vet. Med. Assoc.*, 1976; 169: 1081-1084.
39. Eyster, G.E., Weber, W., Chi, S., Blair, C., Stanley, A., Friedman, H., Soloff, K., Cole, R., Johnston, J.: Mitral valve prosthesis for correction of mitral regurgitation in a dog. *J. Am. Vet. Med. Assoc.*, 1976; 168: 1115-1118.