Clinical Practice Review

Journal of Veterinary Emergency and Critical Care 21(2) 2011, pp 144–150
doi: 10.1111/j.1476-4431.2011.00627.x

Thrombectomy and thrombolysis: the interventional radiology approach

Marilyn E. Dunn, DMV, MVSc, DACVIM

Abstract

Objective – To present interventional therapeutic options for patients with thrombosis.

Etiology – Thrombosis in small animals results from an unbalance in the normal hemostatic mechanisms leading to vessel occlusion. In veterinary medicine, thrombosis is recognized as a common complication of many acquired diseases, including cardiac, endocrine, immunological, inflammatory, and neoplastic disorders.

Diagnosis – Clinical signs are variable depending on the location of the thrombus and various laboratory and imaging modalities can aid in its identification and localization.

Therapy – Once identified, a decision must be made to whether or not intervene and which method is most appropriate. A number of minimally invasive approaches for dealing with thrombosis are available and offer veterinarians a choice of therapeutic options when dealing with a thrombotic patient. In the presence of thrombosis, a combined approach of vessel balloon dilatation, catheter-directed thrombolysis and stenting may be most appropriate. Percutaneous mechanical thrombectomy, if available, may also be appropriate. Embolic trapping devices can be used with vena cava thrombosis to help prevent pulmonary embolism. Anticoagulant therapy may be indicated in the postoperative period to prevent further thrombus formation while the patient's fibrinolytic system breaks the clot down.

Prognosis – Outcome is variable depending on the site of the thrombus formation. Arterial thrombosis can be life-threatening while venous thrombosis tends to be less life-threatening but may lead to pulmonary embolism.

(J Vet Emerg Crit Care 2011; 21(2): 144–150) doi: 10.1111/j.1476-4431.2011.00627.x

Keywords: cats, dogs, therapeutic options, thromboembolism

Introduction

Thrombosis is a major cause of mortality in people with heart disease, cancer, and stroke, and these are the 3 most common causes of death in developed countries.[1] In veterinary medicine, thrombosis is recognized as a common complication of many acquired diseases, including cardiac, endocrine, immunological, inflammatory, and neoplastic disorders.[2] Because of the difficulty in confirming the diagnosis of thrombosis in veterinary medicine, it is highly probably that many patients with thrombosis may go undiagnosed making its true prevalence difficult to estimate. Even when the presence of a thrombus is confirmed, there are numerous limitations related to drug safety and efficacy of treatments that have prompted the development of new therapies, many centering on minimally invasive approaches to thrombosis. A multimodal approach involving a combination of interventional radiology, antithrombotics, anticoagulant therapy, and thrombolytics may hold the most promise for thrombosis management in small animal patients.

Despite numerous reports of thrombosis in small animals, few clinical studies have reported its successful treatment. A few veterinary studies have focused on the use of systemically administered thrombolytics. Thrombolytic drugs target the clot directly by accelerating fibrinolysis. Side effects reported with these agents are bleeding tendencies, pulmonary embolism (when treating venous thromboembolism) and reperfusion injury.[3,4] Tissue plasminogen activator, streptokinase, and urokinase have been used in cats with aortic thromboembolism with generally poor outcomes with survival rates ranging from 35% to 42%.[3–6,a] There

From the Department of Clinical Sciences, Faculté de Médecine Vétérinaire, Université de Montréal, Québec, Canada J2S 7C6.

The author declares no conflict of interest.

Address correspondence and reprint requests to
Dr. Marilyn Dunn, Department of Clinical Sciences, Faculté de Médecine Vétérinaire, Université de Montréal, 1525 rue des Vétérinaires, St Hyacinthe, Québec, Canada J2S 7C6.
Email: marilyn.dunn@umontreal.ca
Submitted July 6, 2010; Accepted January 26, 2011.

are some sporadic reports in dogs involving the use of tissue plasminogen activator, streptokinase, and urokinase with variable results.[3,4,7–9,a] Unfortunately, with the exception of a single recent prospective study of tissue plasminogen activator in cats, prospective controlled clinical studies evaluating thrombolytics and patient outcome are lacking.[10] As an alternative to medical therapy, percutaneous mechanical thrombectomy (PMT) was described and evaluated in a prospective study of 6 cats with distal aortic thromboembolism.[11] The survival rate was 50%, which was similar to conventional medical therapy.[11]

Etiology

Normally, hemostasis is maintained through an intricate balance between endogenous anticoagulants and procoagulants. The net effect is preservation of blood flow in the systemic vasculature with localized coagulation at sites of vessel injury. Changes in this balance can tip the scales to either excessive bleeding or widespread thrombus formation as is the case of true hypercoagulability.[2,12] The primary underlying disorder can influence the site of thrombus formation (eg, arterial or venous vasculature), the composition of the occluding thrombus and the viable therapeutic approaches to thrombus formation. The relative proportions of platelets and fibrin in the clot depend on the shear forces within the injured vessel. Arterial thrombi form under high shear forces and therefore tend to contain a large number of platelets held together by fibrin strands. Venous thrombi form under low shear forces and consist primarily of fibrin and red blood cells. Mixed thrombi are an intermediate form and occur predominantly in the pulmonary vasculature.[2,12,13] Strategies to inhibit arterial thrombogenesis typically include the use of antithrombotics or antiplatelet drugs, whereas anticoagulants are the mainstay of venous thromboprophylaxis.[2,13]

Clinical signs, resulting from compromised blood flow to an organ, can be variable and depend on the affected organ.[13,14] Actual confirmation of the presence of thromboemboli, especially microthrombi, can be clinically challenging to establish. A combination of Doppler ultrasonagraphy, angiography, venography, ventilation perfusion scans, and contrast enhanced CT and MRI imaging can aid in their identification, however, in many cases, microthrombi likely go undiagnosed in small animals.[13]

Treatment

Traditionally, treatment of thrombosis has focused on reducing thrombogenesis or dissolving existing clots through the use of thrombolytics. Reducing thrombogenesis can be achieved with either antithrombotic drugs or anticoagulants. Surgical thrombectomy has only been sporadically reported in the veterinary literature.[15,16] A study of dogs with adrenal tumors and tumor-induced thrombi in the vena cava reported that adrenalectomy and thrombectomy resulted in acceptable outcomes.[15] Another case report documented that a cat with primary hyperaldosteronism and caval thrombus was successfully manage by surgical thrombectomy.[16] To the author's knowledge, surgical arterial thrombectomy has not been reported in the veterinary literature. Patients presenting with arterial thrombosis are often critically ill. The vast majority of cats presenting with an aortic thrombus (the main veterinary example of arterial thrombosis) have significant heart disease and over 50% will present in congestive heart failure thus making them poor surgical candidates.[17]

Minimally Invasive Approaches

By using the technique of catheter-directed thrombolysis, thrombolytic drugs are used to target the clot directly and act by accelerating fibrinolysis. Side effects reported with these agents include bleeding tendencies, pulmonary embolism (when treating venous thromboembolism), and reperfusion injury. These agents can be infused systemically or locally (ie, the agent is delivered through a catheter directly into the affected vessel).[3,4] In people, catheter-directed thrombolytic therapy appears to be associated with better outcomes and fewer bleeding complications for both arterial and venous thrombosis when compared with systemic thrombolytic therapy. Improved outcome associated with this intervention may be due to the fact that the systemic dose is administered at the site of the clot.[14] This technique could prove useful in small animals and is relatively easy to perform in patients with vena caval thrombosis as the thrombolytic agent could be administered through a central line or through a catheter inserted through a central line. A comprehensive review of the systemic use of thrombolytics is beyond the scope of this review and has been extensively reviewed elsewhere.[3–11]

Another important element to consider in the decision making process in a thrombotic patient is the site of the clot. Arterial thrombosis is generally considered an emergency and the time to intervention is critical. Such is the case with aortic thrombosis in cats. Venous thrombosis tends to present less acutely and the decision to intervene may not be as straightforward to make.[18] For instance, if a patient presents with a partially obstructive thrombosis of the vena cava, and the underlying hypercoagulability can be managed, the patient's fibrinolytic system may slowly eliminate the

clot without further intervention. Pulmonary embolism may occur as the clot breaks up.

Balloon Dilatation or Angioplasty

Balloon dilatation or angioplasty of atherosclerotic lesions have been performed for a number of years in human medicine (Figure 1). Angioplasty has been used to plasty clots up against vessel walls thus quickly restoring patency. This technique has mostly been applied to smaller caliber vessels over short segments. Examples of vessels where this technique may be applied include deep vein thrombosis of the femoral or popliteal veins. Some concerns regarding the use of this procedure include reocclusion of the vessel, especially if the patient remains hypercoagulable, and pulmonary embolism during the angioplasty or perioperatively.[14,19,20] In patients at high risk of pulmonary emboli, a caval filter can be placed.

Because of recurrent stenosis following balloon angioplasty other techniques have been investigated to help reduce the occurrence of restenosis. The placement of an endovascular stent in people increases long-term patency rates.[21,22] Another novel approach is the use of drug eluting balloons. Recently, the antiproliferative agent paclitaxel has been used to coat angioplasty balloons to reduce restenosis following balloon dilatation of peripheral artery disease secondary to atherosclerosis.[22] Anticoagulant eluting balloons may prove to be useful in the management of thrombosis in certain veterinary patients.

In order to perform balloon angioplasty in veterinary patients, the vessel must be easily accessible and of sufficient diameter so it does not become completely occluded by the presence of the catheter. Based on the effectiveness of this technique in people, angioplasty may prove to be of benefit in small animal patients with aortic thrombosis as seen in patients with protein losing nephropathy or enteropathy or in cats with cardiac disease and distal aortic thromboembolism. This approach could also be used in patients with cranial vena cava thrombosis secondary to complications following the placement of central venous catheters. To date, a case report describes 2 dogs that presented with pacemaker-induced thrombosis of the cranial vena cava that were successfully treated with catheter-directed thrombolysis and balloon dilatation.[22]

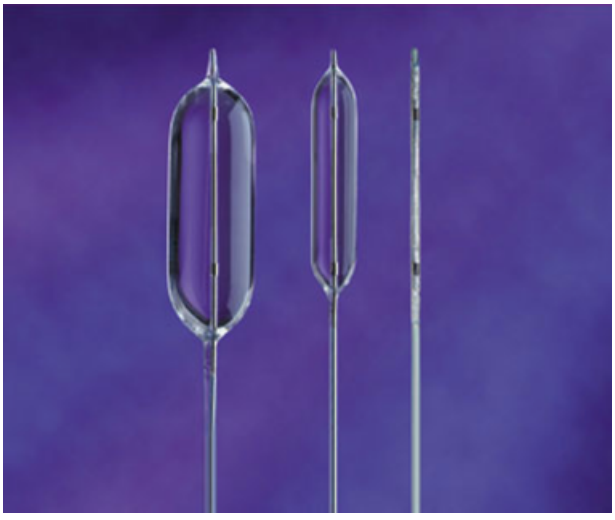

Figure 1: Balloon dilation catheters. Courtesy of Infiniti Medical LLC (Malibu, CA).

Vascular Stenting

Various nitinol-based vascular stents have been developed to treat both arterial and venous peripheral vascular disease including thrombosis in people (Figure 2). Stents are nonthrombogenic and do not appear to be associated with an increased risk of thrombosis at the implantation site; however, as they are often used in hypercoagulable patients, anticoagulants possibly in combination with thrombolytics are most often used.[19,20,23] These stents are routinely used to treat vessel occlusion secondary to atherosclerotic plaques and also used in the treatment of aortic dissection. In people, these stents are placed in the carotid arteries, iliac arteries, renal artery, the celiac, and mesenteric arteries.[24] They have also been used to treat aortic dissection and aneurysms.[23,24] Covered stents or stent grafts consist of a metal exoskeleton covered with a polytetrafluroethylene material, which is impermeable to blood.[23] Stents can be mounted on a balloon or be self-expanding. Some complications reported in people following the use of stents include stent fractures in mobile sites such as upper extremity deep vein thrombosis and femoral and popliteal stenting.[19,23,24] Once in place, vascular stents cannot be removed. Vascular stenting is applicable to veterinary patients and in the future may improve outcome in certain thrombotic conditions as has been demonstrated in people.[21]

Despite the success obtained in people following vascular stenting, up to one-third of patients still undergo stent restenosis. This has led to the development of drug-eluting stents in the hopes of reducing the high rate of restenosis in some patients. Drug eluting stents containing paclitaxel, everolimus and sirolimus have been used successfully in patients with peripheral vascular disease. These agents possess antiproliferative properties that can aid in decreasing vessel fibrosis and therefore may be effective in treating thrombosis and reocclusion.[25]

In small animal patients, there are no published reports of the use of stents specifically to treat thrombotic

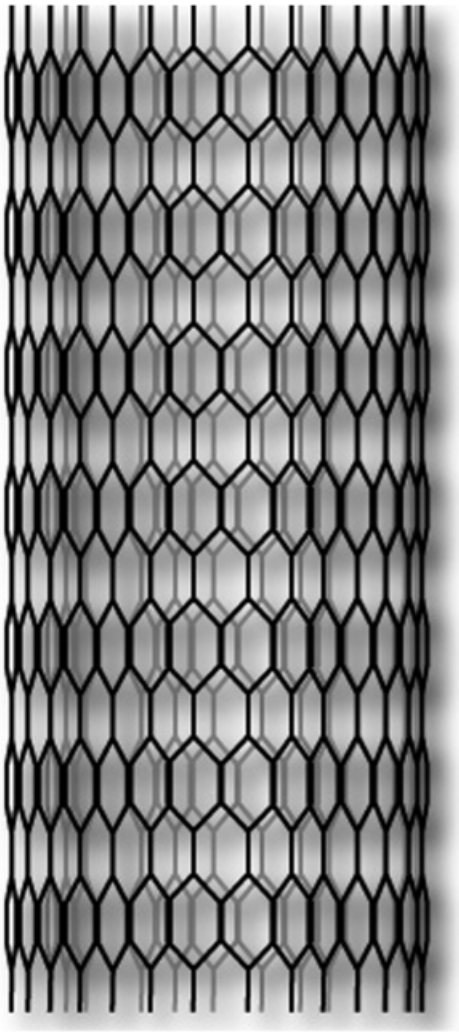

Figure 2: Vascular stent. Courtesy of Infiniti Medical LLC.

disease. The author, along with colleagues, has placed stents in the external iliac arteries extending up and into the distal aorta in a dog that presented with distal aortic thrombosis extending into both external and internal iliac arteries. The procedure was successful and was used in combination with catheter-directed thrombolysis (Figures 3 and 4). The dog recovered full use of the hind legs (except for a gastrocnemius contracture on the left hind limb) and was lost to follow-up 20 months following the procedure. Vascular stents have been placed in the caudal vena of dogs to assist in coil embolization of intrahepatic portosystemic shunts and in the hepatic veins and caudal vena cava in 3 dogs with Budd-Chiari.[26,27] These have been well tolerated and not associated with any adverse effects. A case report of a cat with vena caval obstruction that underwent balloon dilatation and stent placement has also been published.[28]

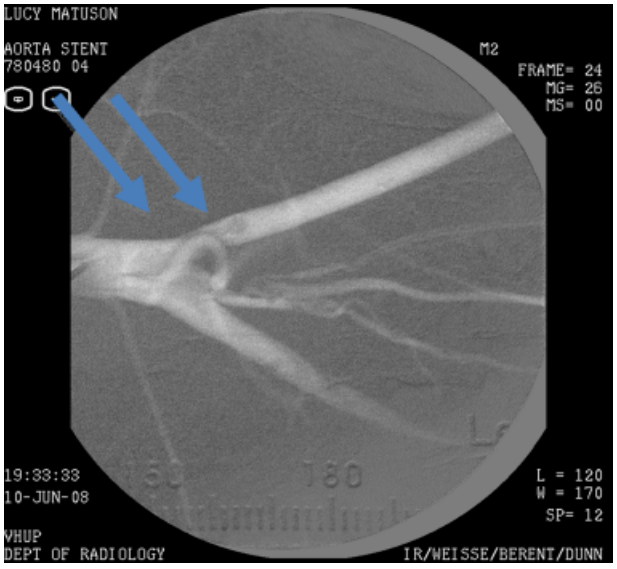

Figure 3: Distal aortogram in a dog with a distal aortic thrombus. Arrows point to filling defects at the aortic trifurcation.

Embolic Trapping Devices

Various devices ranging from baskets to 'spider-like' endovascular implants have been developed in people to trap emboli and prevent them from reaching the lungs. This is particularly important with caval implants in the presence of deep vein thrombosis. Once trapped, emboli can undergo fibrinolysis.[29,30] The most commonly used embolic trapping devices are vena cava filters, which are placed in 3–11% of people with deep vein thrombosis.[30] The use of these filters is indicated when anticoagulant therapy cannot be initiated, must

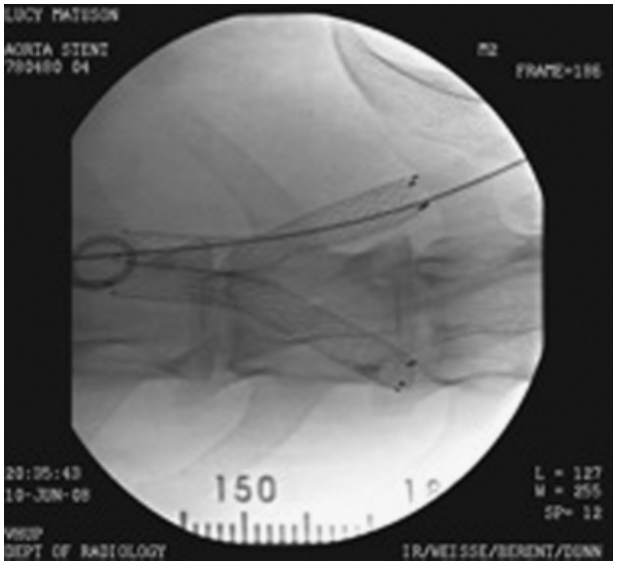

Figure 4: Two caval stents were placed in the external iliac arteries and extending into the distal aorta.

be stopped or is insufficient in protecting patients from pulmonary embolism.[29,30] Filters are most commonly inserted fluoroscopically into the caudal vena cava just under the lowest renal vein in order to trap emboli emanating from the femoral or popliteal veins; however, they may also be placed in the cranial vena cava. Filters can be placed either through the jugular vein or through the femoral vein depending on the desired site of deployment and the size of the patient. Filters must be placed down stream from the clot.[29–33] These devices can be permanent or retrieved once the thrombotic disease is under control. Filters can be made of nitinol or stainless steel and are biocompatible and nonthrombogenic. Some complications reported with these filters include migration and tearing or the perforation of the cava. To the author's knowledge, these devices have yet to be used in clinical veterinary patients. Potential applications in veterinary medicine would be the trapping of emboli from caval clots secondary to adrenal tumors or protein losing nephropathies.

PMT

PMT can be divided into wall contact devices and nonwall contact devices. A nonwall contact device, the Angiojet system,[b] has undergone evaluation in a small number of cats.[11] The Angiojet system emits high velocity saline jets that are directed backwards from the tip of the device to outflow channels creating a localized low-pressure zone (Venturi-Bernoulli effect). These flow jets generate a vacuum force that draws the thrombus back into the catheter. The jets break the thrombus into small fragments that are propelled into the lumen of the catheter and aspirated. Aspiration of these fragments is meant to remove the thrombotic debris without their embolization.[11,20,32] The device must be inserted into the affected vessel and advanced until it reaches the clot and therefore may be size restrictive in some patients. The smallest catheter available for the Angiojet is 4-Fr. Although this system has been used successfully in cats with distal aortic thromboembolism, reperfusion injury was reported following thrombectomy.[11] In human medicine, instead of using saline flush, there are recommendations to use tissue plasminogen activator in the flush to improve thrombolysis at the clot and distal to it.[20,32] This combined approach may improve outcome.

Concurrent Anticoagulant/Antiplatelet Therapy

Following thrombosis intervention, the question of medical anticoagulation becomes important. If the underlying disease that predisposed to hypercoagulability and thrombus formation is not addressed, the patient may thrombose other sites or present recurrence at the same site. In people, many factors are taken into account such as underlying disease, site of the clot and site of the implant, if present, when determining an adequate anticoagulant protocol.[33]

Another consideration is what to do with patients already receiving anticoagulant therapy that must undergo intervention for thrombosis. As bleeding from catheter sites peri- and postoperatively is a concern, it is generally recommended to discontinue anticoagulant and antiplatelet therapy before the procedure. The length of time required for discontinuation of therapy is variable and dependent on the half-life of the agent being used. Based on the short half-life of unfractionated heparin, it can be stopped 2–5 hours before a procedure. Given the longer half-life of low-molecular-weight heparin, these should be stopped 8 hours before a procedure.[34,35] Aspirin causes irreversible platelet inactivation by irreversibly binding cyclooxygenase. Despite its antiplatelet properties, clinical bleeding with aspirin therapy appears to be uncommon.[33] Clopidogrel is a potent antiplatelet medication and complications in people undergoing interventional procedures have been reported. It may therefore be prudent to discontinue clopidogel 7 days before a procedure.[36]

Despite these recommendations, in an emergency situation (eg, arterial thromboembolism) an intervention can be performed despite the use of anticoagulant therapy. The clinician must be prepared for bleeding complications and if needed, be able to reverse the effects of heparin with either protamine or by tranfusion of activated clotting factors in the case of low-molecular-weight heparins.[12]

There is very little information in the veterinary literature on whether to continue anticoagulant and/or antiplatelet medication postoperatively. According to human recommendations, the presence of a vascular stent does not augment thrombogenesis. Anticoagulant/antiplatelet medication should be continued as long as the underlying disease that led to thrombosis is present.[33]

In veterinary medicine, decisions on long-term anticoagulant and antiplatelet therapy are often chosen in regard to ease of administration and cost.

Multimodality Approach

A multimodality approach using systemic anticoagulant therapy, catheter-directed thrombolysis, and endovascular stents may be the most appropriate approach in clinical veterinary patients. A multimodality approach allows direct intervention to rapidly remove the clot or open the vessel lumen while lysing distal clots and preventing further clot formation. This combined approach may result in improved morbidity and mortality. Given the variable presentation and wide range

of underlying disease processes in small animal patients, an individual patient approach will most likely yield the best results.

Prognosis

Prognosis in patients with thrombosis varies depending on the site of the thrombosis, arterial versus venous, the underlying condition which led to hypercoagulability and the clinician's ability to address this underlying condition. Venous thrombosis are generally less life-threatening than aortic thrombosis. Early identification and rapid treatment of thrombotic disease in small animal patients, may improve the prognosis.

Conclusions

Thrombosis in small animals is the result of an unbalance in the clotting mechanism leading to vessel occlusion. Clinical signs are variable depending on the location of the thrombus and various laboratory and imaging modalities can aid in its identification and localization. Once identified, a decision must be made whether or not to intervene and establishing which method is most appropriate to treat the thrombosis. A rapid combined approach of vessel balloon dilatation, stenting, and catheter-directed thrombolysis may be most appropriate for arterial thrombosis. PMT, if available, may also be appropriate. Acute venous thrombosis patients may benefit from balloon dilatation, stenting or catheter-directed thrombolysis. More chronic cases may benefit from embolic trapping devices helping to prevent pulmonary embolism. Anticoagulant therapy prevents further thrombus formation while the patient's fibrinolytic system breaks it down. Given the current paucity of clinical data in this important area, further studies are warranted to determine viable and effective techniques in small animals.

Acknowledgement

The author would like to acknowledge the help provided by Drs. Chick Weisse and Allyson Berent.

Footnote

[a] Whelan MF, O'Toole TE, Chan DL, et al. Retrospective evaluation of urokinase use in dogs with thromboembolism (abstr). J Vet Emerg Crit Care 2005;15(3 suppl 1):S8.

[b] Possis Medical Inc, Minneapolis, MN.

References

1. World Health Organization. World Health Statistics Annual as presented by the United States Census Bureau, Statistical Abstract of the United States, Table 1339. Geneva, Switzerland: World Health Organization; 1997, p. 17.
2. Dunn M. Acquired coagulopathies, In: Ettinger SJ. ed. Textbook of Veterinary Internal Medicine, 7th edn. Philadelphia, PA: Elsevier; 2010, pp. 797–801.
3. Whelan MF, O'Toole TE. The use of thrombolytic agents. Compend Contin Educ Pract Vet 2007; 29(8):476–482.
4. Lunsford KV, Mackin AJ. Thromboembolic therapies in dogs and cats: an evidence-based approach. Vet Clin North Am Small Anim Pract 2007; 37:579–609.
5. Moore KE, Morris N, Dhupa N, et al. Retrospective study of streptokinase administration in 46 cats with arterial thromboembolism. J Vet Emerg Crit Care 2000; 10(4):245–257.
6. Pion PD, Kittleson MD, Peterson S, et al. Thrombolysis of aortic thromboemboli in cats using tissue plasminogen activator. In: Proceeding of the American College of Veterinary Internal Medicine; 1987: San Diego, CA. p. 925
7. Ramsey CC, Burney DP, Macintire DK, et al. Use of streptokinase in four dogs with thrombosis. J Am Vet Med Assoc 1996; 209(4): 780–785.
8. Clare AC, Kraje BJ. Use of recombinant tissue-plasminogen activator for aortic thrombolysis in a hypoproteinemic dog. J Am Vet Med Assoc 1998; 212(4):539–543.
9. Bliss SP, Bliss SK, Harvey HJ. Use of recombinant tissue-plasminogen activator in a dog with chylothorax secondary to catheter-associated thrombosis of the cranial vena cava. J Am Anim Hosp Assoc 2002; 38(5):431–435.
10. Welch KM, Rozanski EA, Freeman LM, Rush JE. Prospective evaluation of tissue plasminogen activator in 11 cats with arterial thromboembolism. J Feline Med Surg 2010; 12(2):122–128.
11. Reimer SB, Kittleson MD, Kyles AE. Use of rheolytic thrombectomy in the treatment of distal aortic thromboembolism. J Vet Intern Med 2006; 20:290–296.
12. Dunn M, Brooks MB. Antiplatelet and anticoagulant therapy, In: Bonagura JD, David C. eds. Kirk's Current Veterinary Therapy XIV. Twedt, PA: Saunders; 2009, pp. 24–28.
13. Darien BJ. Acquired coagulopathy V: thrombosis, In: Schalm's Veterinary Hematology, 5th edn. Philadelphia, PA: Lippincott, Williams & Wilkins; 2000, pp. 574–580.
14. Lin PH, Peden E, Zhou W, et al. Endovascular intervention of iliofemoral venous thrombosis. *Endovascular Today* 2006; 60–66.
15. Kyles AE, Feldman EC, De Cock HE, et al. Surgical management of adrenal tumors with and without associated tumor thrombi in dogs: 40 cases (1994–2001). J Am Vet Med Assoc 2003; 223(5): 654–662.
16. Rose SA, Kyles AE, Labelle P, et al. Adrenalectomy and caval thrombectomy in a cat with primary hyperaldosteronism. J Am Anim Hosp Assoc 2007; 43(4):209–214.
17. Schoeman JP. Feline distal aortic thromboembolism: a review of 44 cases (1990–1998). J Feline Med Surg 1999; 1(4):221–231.
18. McCrory MC, Brady KM, Takemoto C, et al. Thrombotic disease in critically ill children. Pediatr Crit Care Med 2011; 12:80–89.
19. Nemcek AA. Upper extremity deep vein thrombosis: interventional management. Tech Vasc Interv Radiol 2004; 7:86–90.
20. Blum A, Roche E. Endovascular Management of acute deep vein thrombosis. Am J Med 2005; 118:31S–36S.
21. Diehm NA, Hoppe H, Do DD. Drug eluting balloons. Tech Vasc Interv Radiol 2010; 13(1):59–63.
22. Cunningham SM, Ames MK, Rush JE, et al. Successful treatment of pacemaker-induced stricture and thrombosis of the cranial vena cava in two dogs by use of anticoagulants and balloon venoplasty. J Am Vet Med Assoc 2009; 235(12):1467–1473.
23. Chavan A, Lotz J, Oelert F, et al. Endoluminal treatment of aortic dissection. Eur Radiol 2003; 13:2521–2534.
24. Leaney B. What's new in vascular interventional radiology? Aortic stent grafting. Aust Fam Phys 2006; 35(5):294–297.
25. Bosiers M, Cagiannos C, Deloose K, et al. Drug-eluting stents in the management of peripheral arterial disease. Vasc Health Risk Manag 2008; 4(3):553–559.
26. Schlicksup MD, Weisse CW, Berent AC, et al. Use of endovascular stents in three dogs with Budd-Chiari syndrome. J Am Vet Med Assoc 2009; 235(5):544–550.

27. Bussadori R, Bussadori C, Millán L, et al. Transvenous coil embolisation for the treatment of single congenital portosystemic shunts in six dogs. Vet J 2008; 176(2):221–226.
28. Holt D, Saunders HM, Aronson L, et al. Caudal vena cava obstruction and ascites in a cat treated by balloon dilation and endovascular stent placement. Vet Surg 1999; 28(6):489–495.
29. Wholey M, Wu WCL, Toursarkissian B, et al. Embolic protection questions answered. Endovascular Today 2007; June: 67–79.
30. Kaufman JA, Kinney TB, Streiff MB, et al. Guidelines for the use of retrievable and convertable vena cava filters: report from the Society of Interventional Radiology Multidisciplinary Concensus Conference. J Vasc Interv Radiol 2006; 17:449–459.
31. Murphy KD. Superior vena cava filters. Tech Vasc Interv Rad 2004; 7(2):104–109.
32. Murphy KD. Mechanical thrombectomy for DVT. Tech Vasc Interv Rad 2004; 7(2):79–85.
33. Mehta RP, Johnson MS. Update on anticoagulant medications for the interventional radiologist. J Vasc Interv Radiol 2006; 17: 597–612.
34. Mischke RH, Schuttert C, Grebe SI. Anticoagulant effects of repeated subcutaneous injections of high doses of unfractionated heparin in healthy dogs. Am J Vet Res 2001; 62(12):1887–1891.
35. Grebe S, Jacobs C, Kietzmann M, et al. Pharmakokinetik des niedermolkularen Heparins Fragmin D beim Hund. Berl Muench Tieraerztl Wochenschr 2000; 113(3):103–107.
36. Hogan DF, Andrews DA, Green HW, et al. Antiplatelet effects and pharmacodynamics of clopidogrel in cats. J Am Vet Med Assoc 2004; 225(9):1406–1411.