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Use of totally implantable vascular access port with mini-invasive Seldinger technique in 12 dogs undergoing chemotherapy

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ABSTRACT

Vascular access ports (VPAs) are totally implantable devices designed to provide repeated access to the vascular system. Port access is performed by percutaneous needle insertion using a noncoring needle.

VPAs have been placed in 12 dogs affected by different tumors and needing long lasting chemotherapy. Using the non-invasive Seldinger technique a silicone catheter was inserted from the jugular vein up to the junction of the cranial vena cava and the right atrium. The catheter then was connected to the port previously placed in a subcutaneous pocket over the scapula. 7/12 dogs showed no clinical complications. Port was removed in 4/12 dogs for post-operative complications as fistula formation (n.2) and infection/mal-position (n.2). One patient had mild complications shortly after implantation. VPAs were left in site until the death in the rest of patients.

VPAs are useful for dogs undergoing long-lasting chemotherapy protocols as these devices allow peripheral veins to be spared and not seriously damaged for repeated infusion of vesicant drugs. In most cases VPAs are well tolerated and may be left in site for several months.

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1. Introduction

The vascular access port (VAP) was initially developed to deliver chemotherapeutic drugs to human cancer patients (Brincker and Saeter, 1986; Cahalane et al., 2007). VPAs with open-ended catheters are totally implantable vascular access devices designed to provide repeated access to the vascular system for delivering chemotherapeutic drugs, antibiotics, fluids, parenteral nutrition, and blood products. Other uses include plasmapheresis and patient-controlled analgesia; they are also indicated for blood sample withdrawal (Denny, 1993).

The versatility of VPAs has led to their increasing use in numerous applications, including providing access to blood, bile, cerebrospinal fluid, urine and specific organs (Graham et al., 2008). Thanks to the introduction and development of these devices out-patient chemotherapy programs have become routine in humans (Denny, 1993). Implantable ports may be considered the preferred device, compared to central venous catheters, for intermittent drug delivery; also the intact skin cover protects the device from damage, accidental dislodgment and prevents from infection when not in use. Absolute contraindications for VPAs placement include the occurrence of disseminated intravascular

coagulation (DIC) and bacteraemia or septicaemia in the candidate patient (Kock et al., 1998).

In pharmacological and toxicological studies conducted in pre-clinical research the VAP represents an important and useful device which improves animals' overall well-being and reduce experimental stress. In rats, the intravenous drug administration can be performed in different veins, e.g. tail vein, or metatarsal vein, but due to the traumatic injury of the vessel, frequent access to these site is limited. For this reason, implantable device consisting of injection cap, indwelling catheter with fixation wings and silicone tube has been used for repeated intravenous administration (De Wit et al., 2001). Studies conducted in macaques have shown that the most common complications associated to VAP implant were surgical site infection, mechanical catheter occlusion, and wound dehiscence requiring subsequent surgical revision. The permanent VAP enabled macaques to participate completely and enjoy full-time in their social groups (Graham et al., 2009). The application of VPAs did not restrict any species typical behavior such as social grooming, playing, and swimming. A totally implantable catheter-port system enabled the animal to have complete freedom of movement and less stress (Graham et al., 2008; Taketoh et al., 2009).

The scientific literature contains relatively little information about the use of VAP in small animal medicine. In a retrospective study of 172 cases, risk factors associated with the development

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of complications, e.g. sex, propofol administration and vein placement have been described (Culp et al., 2010). The port implant is indicated in those patients candidates to long-lasting chemotherapy protocols or those who have spoiled veins due to prolonged catheterizations or venipunctures (Massari and Romanelli, 2008). VAPs are also used for delivery of drugs, fluids, and parenteral nutrition (Mayer et al., 2008). Dogs and cats affected by neoplastic diseases are suitable candidates for VAP implant which may be inserted into the jugular or femoral vein providing an acceptable means of chronic venous access during chemotherapy (Cahalane et al., 2007; Massari and Romanelli, 2008).

The use of VAPs was also recently reported for feline blood donation (Morrison et al., 2007; Aubert et al., 2011). In cats vascular access ports were effective for frequent collection of small volume of blood. They were extremely well tolerated in 95% of cats and remained patent over one month in 90% of cats (Farrow et al., 2003). Samples collected from VAP are suitable for routine hematologic screening of feline cancer patients even if hemolysis may account for a slight increase in potassium, total protein and albumin concentrations (Henry et al., 2002).

VAPs have been successfully used in dogs receiving external beam radiation therapy for tumor control. This procedure is performed under general anesthesia and requires intravenous catheter placement and spoiled veins management. VAPs implantation in the jugular or lateral saphenous veins markedly reduced time for managing radiation therapy patients (Mayer et al., 2008).

In dogs and cats, port access is performed by percutaneous needle insertion using a non-coring Huber needle. The VAP catheter is most commonly placed into the jugular vein. When placed in this location, complication rates are low and less than 5% requires VAP removal. Femoral location may represent an important option for patients requiring surgery or radiation therapy of the head and neck region (Cahalane et al., 2007).

The VAP can be also used to manage chronic cavitory effusions providing endo-cavitory chemotherapy. In particular a laparoscopic abdominal placement technique has been described for the treatment of a gastro-intestinal stromal tumor (GIST) with peritoneal metastasis in a dog receiving endo-cavitory carboplatin (Massari and Romanelli, 2008).

The present study describes the use of VAPs in 12 tumor-bearing dogs undergoing chemotherapy. Emphasis has been put on describing the non-invasive surgical Seldinger technique for jugular VAP placement (Seldinger, 1953; Nocito et al., 2009). The duration of tolerance to the implanted system, side effects and their management have been reported.

2. Materials and methods

2.1. Animals

Between March 2009 and December 2010, 12 tumor-bearing dogs underwent VAP implantation. Please refer to Table 1 for complete signalment, diagnosis, treatment, date of port placement, chemotherapy protocol adopted, port follow-up, and possible complications observed for each animal.

2.2. VAP device

The VAP device used in this study (BARD® plastic bardport low profile, Bard Access System, Inc., Salt Lake City, UT, USA) consists of two primary components: a 10.0 mm height injection plastic (polyoxymethylene) port with a 10.8 mm diameter self-sealing silicon septum and a radio-opaque silicone or polyurethane 6.6 French catheter (Fig. 1). The silicon septum usually is designed for 1000–2000 access with a non-coring needle (Denny, 1993).

2.3. VAP implantation technique

This technique has been published by Seldinger, in 1953. It consists of catheterization of the selected vein being guided by a fine metallic wire. This technique is considered less invasive compared with the classical one in which the vein is surgically isolated (Seldinger, 1953).

All VAPs before their use should be visually inspected and pressure-tested with saline searching possible defects (Graham et al., 2009). The animals undergoing VPA implantation should be prepared as patients for minor surgery, they should be fasted for 10–12 h, the surgeons and assistant should be prepared by scrubbing and wore sterile gowns, latex surgical gloves, masks and caps. The surgical area should be clipped and aseptically prepared. A 18 G venipuncture needle connected to a syringe is inserted into the external jugular vein; as the vein has been entered, the syringe is removed and the needle left in place. A fine “J-tip” guide-wire is inserted into the needle up to the end of the cranial vena cava. The needle is then removed. A vessel dilator and sheath introducer is advanced using a rotational motion. The locking mechanism is released, the vessel dilator and “J” wire withdrawn whereas the sheath is left in place. At this point the catheter is inserted into the sheath and advanced up to the junction of the cranial vena cava and the right atrium. The correct position of the catheter is assessed using fluoroscopy or ultrasound. The two handles of the peel-away sheath are grasped and pulled outward and upward at the same time until the sheath is completely removed (Fig. 2). A subcutaneous “half-moon shaped” pocket using blunt dissection is created over the dorsal margin of the scapula. A subcutaneous tunnel from the port pocket site to the venous entrance site is created using a tunneler. The tip of the tunneler is advanced from the port pocket site to the venous entry site. The catheter tip is then threaded onto the end of the tunneler and the latter is pulled back to the port entry site. At this point the catheter is connected to port. The port is placed in the subcutaneous pocket away from the incision line and is secured to underlying fascia using monofilament absorbable suture material such as 3-0 polydioxanone (PDS) to prevent it flipping in the pocket. The catheter is tested using a non-coring needle connected to a 10 ml syringe containing heparinized 0.9% saline to confirm that the flow is not obstructed and that the catheter is correctly positioned (Fig. 3).

The incision site is closed in a routine manner. Soon after the port has been placed, a thoracic radiograph in lateral recumbency is performed in order to assess the correct position of the catheter at the junction of the cranial vena cava and the right atrium (Fig. 4). The overall procedure time is about 30 min.

The dog, the day after port placement, is fully re-evaluated to check its clinical status and patency of the catheter. The patency of the VAP is maintained by flushing the port before each chemotherapy administration. In preparation for flushing, the hair-coat over the port is always clipped and the skin surgically prepared to decrease the possibility of infection. After testing the patency of the system, chemotherapeutic drugs are administered connecting the infusion set to the Huber needle (Fig. 5). In case of systemic signs of infection, overt mal-position (Fig. 6) or fistula of the port, removing the VPA is advisable.

The VAPs implanted were also used for blood withdrawal in order to collect a small sample for complete blood count (CBC) before the administration of chemotherapeutic agents. Generally about 3 ml of blood initially collected was discarded before using it to fill the EDTA vial.

Removal of the port is performed by sharp dissection through the old incision and through the fibrous capsule that develops around the port. As soon as the catheter is removed, a mild pressure procedure is applied in the area so the walls of the vein collapse each other preventing blood outflow from the catheter access site.

Table 1
Signalment, diagnosis, treatment, date of port placement, chemotherapy protocol adopted, port follow-up, and possible complications observed for each animal included in the investigation.

No.	Breed	Age (year)	Sex	Diagnosis	Treatment	Date of VPA placement	Chemotherapy protocol and administration route	Port follow-up	Complications
1	Corso	3	FS	Anaplastic sarcoma in the chest wall	En bloc resection + adjuvant chemotherapy	03-11-2009	Doxorubicin, iv	Still in place at euthanasia due to spinal metastasis 05-30-2009	None
2	Husky	8	FS	Abdominal HSA	Mass removal + adjuvant chemotherapy	03-18-2009	Doxorubicin liposomal, iv + dacarbazine, iv	Removed 06-20-2009	VPA mal-position, infection (<i>Pseudomonas</i> spp.)
3	Bernese mountain dog	7	M	Multicentric lymphoma	Chemotherapy	04-08-2009	COPLA*	Removed 04-29-2009	VPA mal-position, infection (<i>E. coli</i>)
4	Golden retriever	10	MI	Orbital OSA	En bloc resection + adjuvant chemotherapy	04-22-2009	Carboplatin, iv + doxorubicin, iv	Still in place at euthanasia due to relapse 05-22-2009	None
5	Husky-like	12	FS	Hepatocellular carcinoma	Hepatic lobectomy + adjuvant chemotherapy	06-10-2009	Doxorubicin, iv	Still in place at euthanasia 09-14-2009	None
6	Dobermann	8.5	F	Proximal tibia OSA	Amputation + adjuvant chemotherapy	9-04-2009	Carboplatin, iv + doxorubicin, iv	Still in place at euthanasia 06-04-2010	None
7	Cross-breed	8	M	Splenic HSA	Splenectomy + adjuvant chemotherapy	12-02-2009	Doxorubicin, iv + thalidomide, po	Still in place at euthanasia 06-11-2010	None
8	Labrador retriever	6	M	Splenic HSA	Splenectomy + adjuvant chemotherapy	12-07-2009	Doxorubicin liposomal, iv + dacarbazine, iv + thalidomide, po	Removed 04-22- 2010	VPA fistula
9	Cross-breed	9	M	Appendicular OSA	Amputation + adjuvant chemotherapy	12-07-2009	Carboplatin, iv + doxorubicin, iv	Still in place at euthanasia due to metastasis 02-12-2010	None
10	American bulldog	10	M	Maxillary OSA	Maxillectomy + adjuvant chemotherapy	02-10-2010	Carboplatin, iv + doxorubicin, iv	Still in place at euthanasia 09-15-2010	None
11	Pitbull	9	F	Multicentric lymphoma	Chemotherapy	07-22-2010	W/M**	Removed 07-13-2011	VPA fistula
12	Rottweiler	9	F	Multicentric lymphoma	Chemotherapy	10-11-2010	W/M**	Still in place at euthanasia 10-03-2011	Post-surgery infection; good recovery with antibiotics

List of abbreviations used: F, female intact; FS, female spayed; M, male intact; HSA, hemangiosarcoma; OSA, osteosarcoma; iv, intravenously; po, per os; sc, subcutaneously; *COPLA, cyclophosphamide, po, vincristine, iv, prednisone, po, L-asparaginase, sc, adriamycin-doxorubicin, iv; **W/M, Wisconsin/Madison protocol.



Fig. 1. Plastic bardport low profile. A 10.0 mm height injection plastic (polyoxymethylene) port with a 10.8 mm diameter self-sealing silicon septum is connected to a radio-opaque silicone or polyurethane 6.6 French catheter.

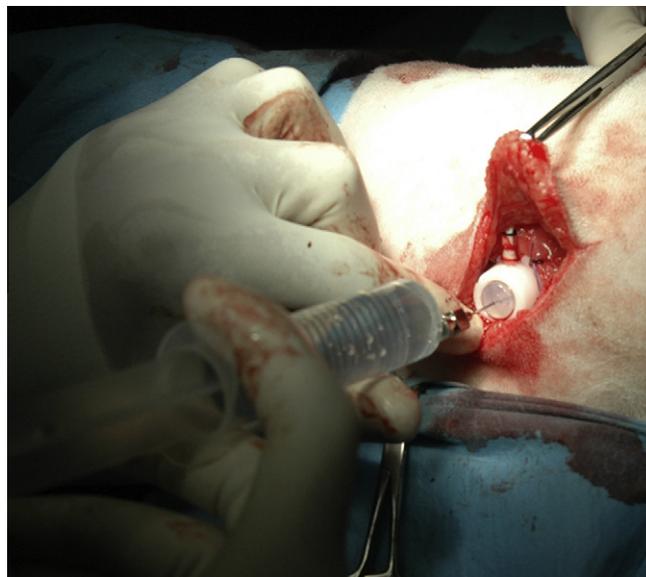


Fig. 3. Procedure of VPA implantation in the dog. Testing the catheter using a Huber needle connected to a syringe containing heparinized 0.9% saline before to close the incision site.

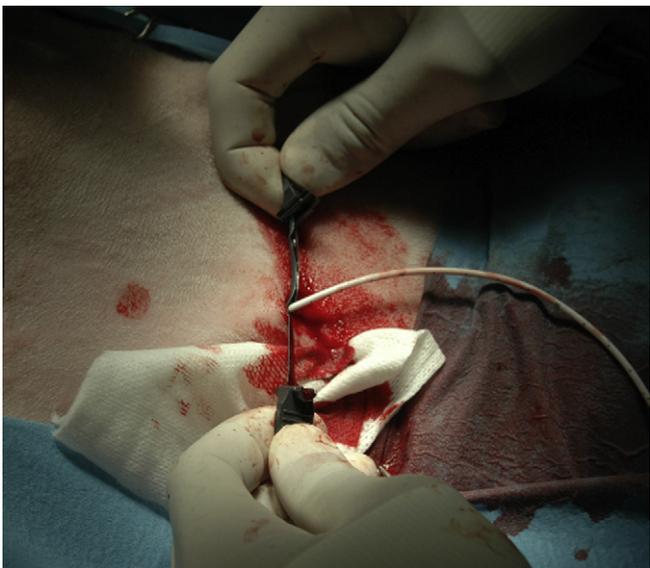


Fig. 2. Procedure of VPA implantation in the dog. Removal of the peel-away sheath once the catheter has been inserted in the vein.

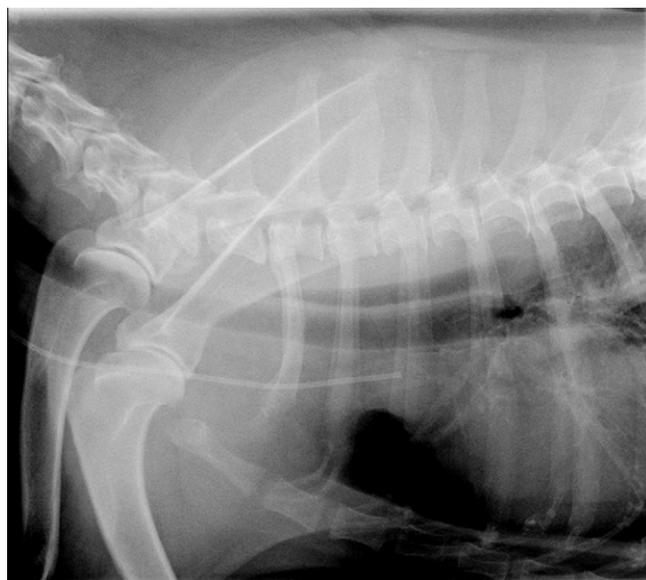


Fig. 4. Lateral thoracic radiograph showing the correct position of the catheter tip at the junction of the cranial vena cava and the right atrium.

3. Results

Vascular access ports have been placed in the external jugular vein of 12 medium to large breed dogs ranging from 22 kg up to 50 kg (6 males and 6 females) receiving chemotherapy as a primary treatment or adjuvant to surgery (Table 1). These patients were affected by a wide range of neoplastic diseases (4 osteosarcoma, 3 multicentric lymphoma and hemangiosarcoma, 1 anaplastic rib sarcoma, 1 hepato-cellular carcinoma). None of these patients showed complications during or immediately after port implantation except one dog, which developed gastrointestinal hemorrhagic diarrhea soon after port placement. This dog fully recovered after a short course of wide spectrum anti-bacterial drugs (amoxicilline/clavulanate 20 mg/kg bid PO and metronidazole 15 mg/kg bid PO) plus symptomatic treatment (anti-diarrhea



Fig. 5. Clinical application of the VAP. A chemotherapeutic drug is infused through the implanted VAP.



Fig. 6. Lateral thoracic radiograph showing a case of VAP mal-position with the catheter entering the right atrium.

compounds, enteral probiotics supplementation). None of dogs included in the study showed sign of discomfort of the implanted port in the following period. On the other hand an increased skin nociceptive sensitiveness to the Huber needle insertion at the port implantation site was noticed; indeed, many dogs had distress or pain reactions during the insertion of the needle from the skin to the silicon septum of the port. This differs from a previous work in which only few patients showed evidence of pain or discomfort during transcutaneous port puncture (Massari and Romanelli, 2008). Only two patients developed intermittent fever, weakness and anorexia after 3 weeks (case number 3) and after 3 months (case number 2). In both patients the port was removed and cultured with positive bacterial outcome (*Escherichia coli* and *Pseudomonas* spp.). Based on the sensitivity testing dogs were treated with Ceftriaxone 20 mg/kg SC sid for about 10 days. Eight dogs arrived to euthanasia with the port still in place. Two dogs had the port removed after 1 year (case number 11) and 5 months (case number 8) respectively for subcutaneous port fistula. One dog (case number 12) showed post-surgery moderate fever suggesting infection that recovered promptly after a short course of antibiotic (amoxicilline plus clavulanate).

4. Discussion and conclusions

Based on this retrospective case series, VAP system should be considered as a very useful and un-stressful device to deliver chemotherapeutic agents to tumor-bearing dogs. In human medicine VAPs are inserted in local anesthesia with minimum surgical time required. On the other hand in veterinary medicine the procedure must be performed under general anesthesia. Due to the Seldinger technique described in our study, the surgical time was very low, with a minimally invasive procedure allowing a very rapid recovery of patients. Once implanted, VAP was very well tolerated and no dogs had functional limitations or implant-dependent distress. The increased skin nociceptive sensitiveness to the Huber needle insertion at the port implantation site was the only side effect reported. In human medicine, this unpleasant feeling is overcome by using local anesthetic gel and it might be a valid option in veterinary medicine as well. In our case series no anesthetic gel has been used for this purpose.

In our opinion there are many advantages related to the use of VAP:

- many chemotherapeutic drugs are vesicant when administered via the peripheral venous route and the extravasation of these agents can cause extensive subcutaneous tissues injuries. VAPs, by-passing peripheral veins, avoids this serious complication;
- the use of VAP may also spare peripheral veins and the pain of repeated needle sticks.

Even if the administration of chemotherapeutic agents by means of VAP is quicker and safer compared with the peripheral venous catheter system, the operator should follow the same chemo-safety guidelines preventing contamination of environment and personnel from toxic effects.

In human medicine, VAPs are mainly implanted by anesthesiologists and medical oncologists, less frequently by surgeons. The non-invasive procedure described above should be part of the veterinary oncologist knowledge and skills with an emphasis on their training in placement and management of VAPs. Moreover, people undergoing long-lasting chemotherapy experience have a port implanted; the authors believe that it should be the future trend for veterinary patients. Regarding the side effects of VAPs, the most common complication is the catheter-related thrombosis occurring in 3.7–10% of human patients (Denny, 1993). This inconvenience may be related to the hypercoagulability state, which usually occurs in most of the oncology patients. Other factors promoting thrombosis include venous irritation caused by some chemotherapeutic agents. In experimental animals catheter placement at the junction between right atrium and cranial vena cava demonstrated reduction in the risk of venous thrombosis. It has been suggested that trauma of the endothelial surface, can be prevented by placing the catheter tip at this site level where the blood flow is increased compared with that of the cranial vena cava (Gebhardt et al., 1997). Catheters suspected of tip occlusion by a fibrin sheath or thrombus should be promptly treated with a fibrinolytic agent such as urokinase (Denny, 1993).

The second most common VAP-related complication reported in human medicine is the blood-stream infection. It can occur both early or late in the therapy, with serious consequences despite the availability of specific antibiotics identified by culture. Many patients are immune-compromised because of the underlying disease, immunosuppressive therapy or chemotherapy and they are at higher risk for infection (Denny, 1993; Cahalane et al., 2007). In small animal veterinary oncology the above-mentioned complications are less frequent. Indeed, several dogs with terminal illness are euthanized with their port implanted with no signs of complications (Massari and Romanelli, 2008) as also reported in this case series. In veterinary oncology, blood-stream infections seem to be more frequent than venous thrombosis compared to humans. This seems to be due to the abundance of skin and coat bacterial populations responsible for microbial catheter colonization (Seguela and Pages, 2011) associated with poor host immune defense of tumor-bearing dogs. Infections may be due to neutropenia, contamination during surgical procedure or during venipuncture of the silicone septum with non sterile non-coring needle (Seguela and Pages, 2011).

In our experience two dogs showed signs of systemic illness including fever, inappetence and lethargy due to infection caused by *E. coli* and *Pseudomonas* spp. respectively. After port removal and antimicrobial therapy based on sensitivity testing both dogs completely recovered.

In conclusion, in this study, vascular access ports have been implanted using the mini-invasive Seldinger technique. This procedure avoids blunt dissection to expose the vein and the J-tip wire guide is used to enter the vessel with minimal tissue injury. Both the surgical and recovery time were shorter compared with the traditional technique. VAPs are very useful for patients undergoing long-lasting chemotherapy protocols. These devices prevent

peripheral veins damage from repeated venipuncture and drug injection or infusion, above all, of vesicant drugs. The implant, when properly placed, is well tolerated and may be left in site for several months. In this study many patients underwent euthanasia after several months from their primary treatment; these patients have the VAP still in place, which did not cause any discomfort. This study prompts the veterinary oncologist to adopt the VAP system in order to reduce the chemotherapy administration time and to improve management and quality of life of dogs receiving anti-cancer drugs mainly when peripheral veins are totally spoiled and difficult to catheterize after a multiple use.

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