Int J Clin Exp Med 2015;8(1):744-750
www.ijcem.com /ISSN:1940-5901/IJCEM0003130

Original Article

Feasibility study on the application of fenestrated stent grafts in canine aortic arches

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Received October 13, 2014; Accepted December 9, 2014; Epub January 15, 2015; Published January 30, 2015

Abstract: Objective: To validate the feasibility and effectiveness of applying fenestrated stent grafts in canine aortic arches. Methods: According to the anatomic characteristics of the aortic arches from four adult beagle dogs, a straight-type aortic coated vascular stent system from Lifetech Scientific (Shenzhen) Co., Ltd. was released in vitro, after which a square window was burnt out at the back tendon of the coated vascular stent with an electrocautery pen, and the fenestrated stent grafts were then returned in the catheter and delivery sheath, following the original release path. Endovascular aortic repair (EVAR) was then performed in the canine aorta. Immediately after surgery, digital subtraction angiography (DSA) and computed tomography (CT) angiography were conducted. On day 3, the dressing was changed, and on day 7, the stitches were removed and CT angiography was reviewed. Animal autopsies were performed 2 weeks after surgery. Results: DSA and CT angiography were conducted in 4 beagles immediately after the experiments. The CT angiography reviewed on day 7 after surgery and the animal autopsy performed two weeks after surgery both revealed that the fenestrated stent grafts were anchored in the canine aortic arch, the openings were aligned against the branch vessels above the aortic arch, and in each branch vessel, the blood flow was smooth, without any obvious internal leakage phenomena. Conclusion: An ordinary straight-type coated vascular stent, fenestrated in vitro, followed by the performance of EVAR in the canine aortic arch for in vivo stent implantation, was technically feasible. When a branch coated vascular stent cannot meet the individual needs of the wound, this technology may provide a valuable strategy for clinical thoracic aortic trauma emergencies.

Keywords: Endovascular repair, stent, aortic dissection, fenestration

Introduction

The endovascular aortic repair (EVAR) procedure that has arisen in recent years is not only minimally invasive but also has a simple preoperative preparation procedure with fewer complications. Additionally, EVAR has better indications in descending thoracic aortic dissection and other vascular diseases. However, due to its special anatomical location, the aortic arch artery involves three major blood vessels on the arch-the innominate artery, the left common carotid artery and the left subclavian artery, making EVAR of aortic arch diseases one of the most challenging research projects in the current cardiovascular surgery field [1, 2]. Especially in cases of rescue of thoracic aortic trauma (TAT) with EVAR, some technical limitations remain throughout the world [3].

The main technical limitation of this procedure is that when thoracic aortic trauma involves the aortic arch branch vessels, especially in the last section of the arch, the existing vascular stents cannot meet the needs of the clinical emergency. In this study, the existing straight-type coated vascular stents were fenestrated and transformed in vitro on site and were then returned in the catheter and delivery sheath, making them suitable for canine aortic arches, which validated the safety and effectiveness of applying fenestrated stent grafts in the endovascular repair of canine aortic arches.

Materials and methods

Materials

Between March 2012 and August 2012, four adult experimental beagles were selected. They weighed 10.5~13 kg, with an average of 11.5 kg. The animals were fed and maintained by specialists in the department of Experimental Medicine, Wuhan General Hospital of Guang-

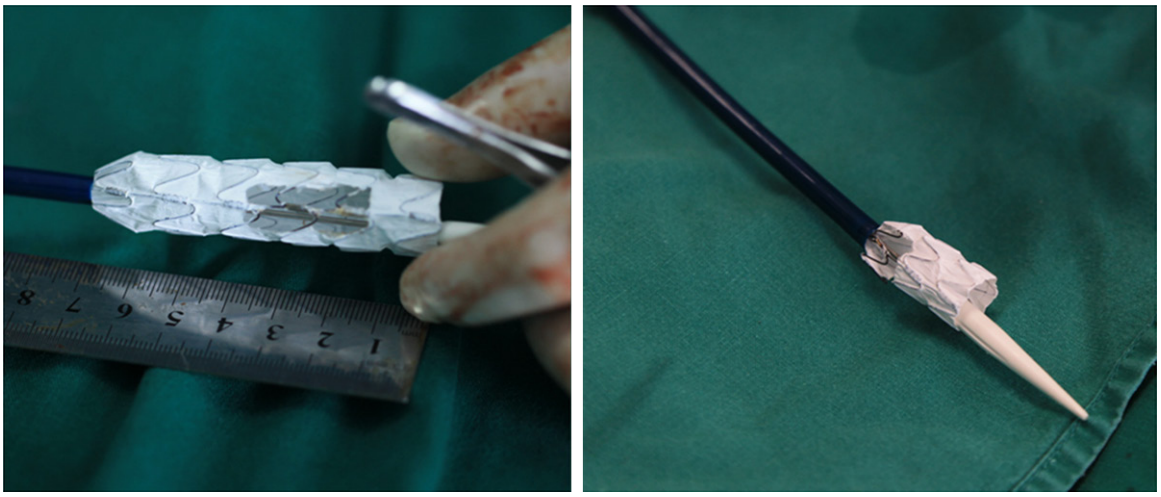

Figure 1. Picture of coated vascular stents made into fenestrated stent graft (a) and returned in the catheter and delivery sheath.

zhou Command. All animals were reared for at least one week before the experiment.

Instruments

One set of commonly used thoracotomy surgical instruments (disinfected by the sterile supply department, Wuhan General Hospital of Guangzhou Command), noninvasive vascular clamps, medium spreaders, 6-0 prolene threads (Johnson & Johnson Medical Devices Co., Ltd., China), and 2-0 and 1-0 common threads (Johnson & Johnson Medical devices Co., Ltd.) were used.

Equipment

A U.S. Newport E200 ventilator, electrocardiogram (ECG) monitor, oximetry cables, and a spiral computed tomography (CT) scanner (Japan Toshiba Aquilion 16 Slice, 4X74-D07951) were used. An X-ray imaging system (U.S. OEC9800), a SIMMON Angiographic Catheter, a 4 F arterial sheath, a gold-marked pigtail catheter, a 90-cm-long metal sheath, a 180-cm loach guide wire, an 18 F conveyor provided by Lifetech Scientific (Shenzhen) Co., Ltd., a thoracotomy surgical instrument package, and a vascular surgical instrument package were all disinfected by the sterile supply department of Wuhan General Hospital of Guangzhou Command.

Narcotic drugs

Ketamine, propofol, fentanyl, vecuronium, chloral hydrate solution and atropine were provided by Department of Anesthesiology, Wuhan General Hospital of Guangzhou Command. Use of the medication was under the supervision and guidance of clinical anesthesiologists.

Other drugs

A cefazolin sodium injection needle (Harbin Pharmaceuticals Second Factory, Lot: 970813), 10 U/100 ml heparin (Nanjing Xinbai Pharmaceutical Co., Ltd.) saline, and a 76% compound meglumine diatrizoate (Xudong Haipu Pharmaceutical Co., Ltd., China) were used.

Experimental methods

Preoperative preparation and anesthetic methods: The beagle aneurysm model was established after one week of regular feeding, and no food or water was given 24 h before surgery; the beagles were weighed, and their body weights were recorded. Two hours before surgery, 5 mg/kg ketamine was injected intramuscularly. The dog's tongue was pulled out using an oval clamp after the onset of anesthesia. The skin was cleaned, the abdominal skin was prepared for a double forelimb axillary artery puncture site, and cefazolin sodium for injection was used for the skin test. Intravenous access was established in the dog's forelimbs. Intravenous infusion was performed with 1.0 g of cefazolin sodium for injection diluted in 100 ml saline. Anesthesia was performed in a catheter lab, an intramuscular injection of 5 mg/kg ketamine was applied, and the anesthesia was

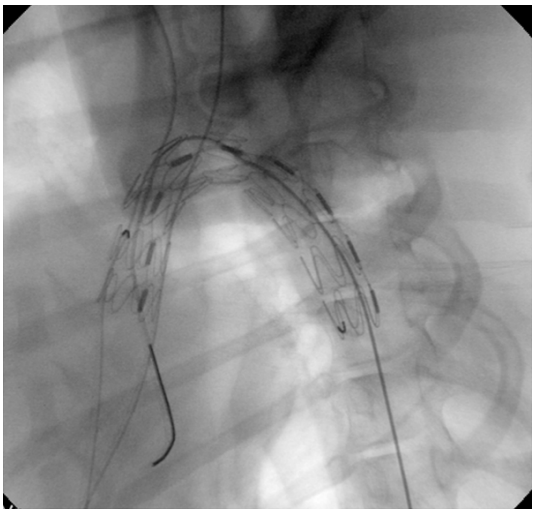

Figure 2. DSA revealed that the fenestrated stent grafts were released successfully, with good blood flow in the aortic arch branch vessels and with no obvious internal leakages in the vascular stents.

induced by slow intravenous injection of 0.5 mg atropine, 30 mg propofol and 1 mg vecuronium. After the anesthesia took effect, physical activity decreased and gradually disappeared, the eyeballs were fixed, and corneal reflexes slowed and disappeared. Tracheal intubation was performed rapidly, a special central circular padded denture was inserted, and a respirator was connected. Ventilator parameters: A synchronized intermittent mandatory ventilation (SIMV) breathing pattern was used, with tidal volume (VT) 32 ml/kg, inspiratory/expiratory time ratio 1:0.8, respiratory rate (RR) 20 beats/min, and inhaled oxygen concentration (FiO_2) 80%. One side of the dog's tongue was pulled out with an oval clamp. Continuous intravenous infusion of 0.1 mg/(kg min) propofol was administered to maintain anesthesia, and if necessary, additional fentanyl was added 0.05 mg at a time.

Fenestrated stent grafts (FSGs): The straight-type coated vascular stent model was selected based on measurement of the results from surgery for establishing the canine aneurysm model and from postoperative CT angiography (CTA) examination. This group chose straight-type coated vascular stents 16 mm in diameter. The fenestration stent grafts were prepared at the time of EVAR: after the release of the aortic stent system graft from Lifetech Scientific (Shenzhen) Co., Ltd. in vitro, a square window (approximately 8 mm × 25 mm, as shown in

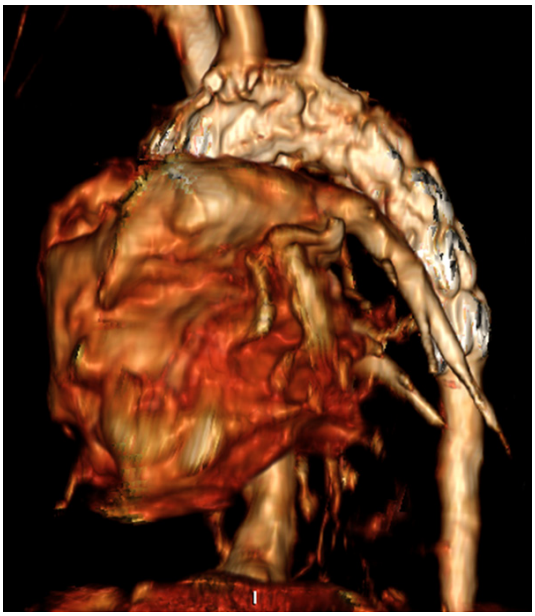

Figure 3. CT angiography revealed a successful release of fenestrated stent grafts.

Figure 1) was burnt out with an electrocautery pen at the back tendon of the coated vascular stent according to the anatomical characteristics of the canine aortic arch. The fenestrated stents were then returned in the catheter and delivery sheath along the original release path.

EVAR method: After preoperative preparation was completed, EVAR was conducted in the catheter lab. Under general anesthesia and with ECG monitoring, the left and right axillary arteries were punctured and placed in the arterial sheath, and a pigtail catheter and marked guide wire were introduced into the ascending aorta and labeled for later use. The abdominal aorta was exposed and punctured, followed by the placement of the arterial sheath, pigtail catheter, and marked guide wire traction into the ascending aorta. After angiography confirming the opening position of the aortic branch vessels, the abdominal aorta was blocked, cut open, and then replaced with a 0.035-inch Amplatz super-hard guide wire. The air in the stent grafts was removed in vitro along the superhard guidewire, and the coated vascular stent was pushed forward slowly to the ascending aorta under fluoroscopy. Under digital subtraction angiography (DSA), the fenestrated stent grafts were released, and the openings were aligned against the canine aortic arch branch vessels. Angiography showed good blood flow in the canine brachiocephalic and

Figure 4. Postoperative animal autopsy indicated that the fenestrated stent grafts were released successfully.

left subclavian arteries. When the delivery sheath was withdrawn, angiography was repeated to confirm good blood flow in the brachiocephalic and left subclavian arteries, with no obvious internal leakages. The blood flow in the abdominal aorta was restored, and 6-0 prolene thread was used to repair the abdominal aorta, suturing layer by layer to close the abdomen.

Postoperative management: The surgery was completed under general anesthesia, and the anesthetized beagle dogs were given tracheal intubation and external simple breathing balloons. The dogs were placed in an air-conditioned doghouse with a room temperature of 30°C after the CT angiography examination. Tracheal intubation was removed after the dogs awakened from the general anesthesia. The venous access was removed after the dogs could stand by themselves, and the dogs were put back into their cages. Postoperative cefazolin sodium 1.0 g/d was administered for three days to prevent infection, while nutritional support was strengthened. On day 3 after surgery, the dressing was changed; on day 7, the stitches were removed; and animal autopsies were conducted two weeks after surgery.

Results

The experiment proceeded smoothly. Instant DSA and CT angiography, the review of CT angiography on day 7 after surgery, and the animal autopsies two weeks after surgery in the 4 beagles all revealed that the fenestrated stent grafts were anchored in each canine aortic arch, and their openings were aligned against the branch vessels above the aortic arch, with good blood flow in each branch vessel and without obvious internal leakage phenomena (**Figures 2**-**4**).

Discussion

Thoracic aortic traumatic conditions are critical and can change rapidly, with on-site mortality rates as high as 80%. The mortality rate of the wounded taken to the hospital is still 30% without an active and effective treatment [3-5]. Traditional treatment is thoracotomy surgical repair and/or artificial blood vessel replacement; however, surgical trauma can be large, large amounts of blood can be needed, and the incidence of complications is high [3]. For example, the surgery must often be conducted under extracorporeal circulation, which requires systemic heparin; if combined with injury to other organs, heparin will aggravate wound bleeding. Thus, rapid, simple and convenient treatment methods have been explored [6, 7].

In the EVAR procedure that has arisen in recent years, intervention materials (such as coated vascular stents) are placed in aortic blood vessels through percutaneous vascular puncture, the vascular damage site is sealed from the cavity, and the vascular integrity is restored. Unlike traditional surgery, thoracotomy or cardiopulmonary bypass is not needed, and the procedure can be completed under local anesthesia. EVAR has the advantages of low anesthetic risk, short operative time, little trauma, little blood loss and few surgical complications, and vascular imaging examination and the rescue process of coated vascular stent placement can be conducted quickly (i.e., diagnosis and treatment can occur in one visit), resulting in a significantly improved success rate [8, 9]. EVAR was first applied in the treatment of descending aortic dissecting aneurysms and true aneurysms [10]. With the subsequent and continued improvement of surgical techniques, continuous improvements in stent technology and increasing accumulations of experience, EVAR has been tested in the treatment of aortic arch diseases [11, 12]. This method may also be suitable for wounded individuals with tho-

racic aortic trauma to stop bleeding quickly, with one-stop rapid endovascular repair and an immediate first-aid effect. Thus, EVAR may provide a feasible solution for rescuing critically injured individuals with traumatic ruptures of the thoracic aortic vessels.

However, current technology may not yet be able to treat vascular diseases and reconstruct the aortic arch entirely through EVAR. The main reason for this limitation is that the anatomic site of the aortic arch artery is special and involves three major blood vessels above the arch - the innominate artery, the left common carotid artery and the left subclavian artery-making EVAR of aortic arch diseases one of the most challenging research projects in the current field of cardiovascular surgery [3]. There are still certain technical limitations to this procedure throughout the world, especially in thoracic aortic trauma emergency treatment with EVAR. The main technical limitation is that some variation exists in the anatomical structures of important branch blood vessels above the aortic arch [13, 14]. This variation requires that the coated vascular stent models for this site be varied and individualized. Although reports exist in which branch vascular stents, "chimney" vascular stents, "modular" vascular stents, EVAR of customized vascular stents and "hybrid" surgical approaches were used, due to the high variation of the aortic arch branch vessels, preparing their corresponding individualized coated vascular stents is a lengthy process, and thoracic aortic trauma is a critical disease whose treatment cannot be delayed [15-17]. Thus, the application of EVAR in the treatment of thoracic aortic trauma is limited.

In recent years, a few scattered cases have been reported that after the coated vascular stent system was released in vitro, according to the anatomic characteristics of the aortic, a square window was burnt out in the back tendon of the coated stent (as shown in **Figure 1**) with an electrocautery pen. The fenestrated stent was then returned in the catheter and delivery sheath, made into fenestrated stent grafts to reserve a blood flow channel for the aortic branch blood vessels, and then released in the aorta with the EVAR technique to solve this problem [18, 19].

This study, using dogs as the study subjects, validated that after the existing straight-type coated vascular stent was released in vitro, according to the anatomical characteristics of the aortic arch, a square window was burnt out in the back tendon of the coated stent with an electrocautery pen (**Figure 1**). The fenestrated stent was then returned in the catheter and delivery sheath. The prepared fenestrated stent grafts may be adapted to the treatment of canine thoracic aortic trauma of the aortic arch, as they were designed to provide new ideas and experimental evidence for the selection and manufacture of stents in the clinical treatment of thoracic aortic trauma.

Fenestrated stent grafts have several advantages. Firstly, the physician can use the EVAR technique alone for the treatment of thoracic aortic trauma involving the aortic arch and even other aortic diseases without "hybrid bypass" surgery and an additional thoracotomy. Secondly, stents do not need individual customization by manufacturers, only requiring the fenestration reconstruction of an ordinary straight vascular stent. This fenestration reconstruction technology is easily mastered by clinicians, and the reconstruction only takes approximately 10 minutes. Thirdly, the use of fenestrated stent grafts is not restricted by the variation of the aortic arch branch vessels. Fourthly, the release of fenestrated stent grafts is a simple operation that does not involve the re-release, docking, etc. (such as "chimney" technology, "hybrid" technology) and other complex procedures of coated stents of aortic arch branch vessels. Fifthly, the cost of fenestrated stent grafts is low, as they only require the transformation of an ordinary straight-coated stent; thus, the cost is significantly lower compared to the cost of "chimney" stents and branch stents.

Several issues should be noted regarding EVAR surgery. Firstly, the coated stent needs to be released in vitro before the fenestration. It should be noted that the coated stent cannot be fully deployed during release. At least 1/3 of the coated stent should remain in the delivery sheath; otherwise, it would be difficult to return the coated stent to the delivery sheath. Secondly, after the coated stent is fenestrated in vitro, withdrawing it to the delivery sheath may not be easy; the coated stent may be tied with 2-0 threads and returned to the delivery sheath by an assistant. Thirdly, although it is not easy for coated stents to return to the deliv-

ery sheath after fenestration, the operator should still mark the fenestration size, scope, and its relationship to the back tendons of the coated vascular stents. Errors in the in vivo release position of the "window" for the coated stents should be prevented; additionally, the direction of a coated stent must not be twisted when it is returned to the delivery sheath, or it would be vulnerable to closing the opening of the aortic arch branch vessels. Fourthly, the coated stent fenestrated "window" should not be too wide; otherwise, it is prone to experiencing complications involving internal leakage and would not be able to achieve the goal of isolating an aneurysm rupture when used clinically.

The difficulty in this experiment was the positioned release of the fenestrated stent graft "window". Thus, left and right axillary artery punctures were applied in the experiment, and double-marked guidewires were placed. In EVAR, the three marked guidewires, including the double-marked guidewires and the marked guidewire placed within the femoral artery puncture, were defined as "++" with marked guidewire systems. On the one hand, these marked guidewire systems may pinpoint the openings of the brachiocephalic and left subclavian arteries; on the other hand, the two marked guidewires from the left and right axillary artery punctures may help build the blood flow in the brachiocephalic and left subclavian arteries. If deviation of the fenestrated stent graft occurs, it may be further corrected through these two marked guidewires. Additionally, the blood flow in two major arteries, the brachiocephalic and the left subclavian, may be validated after the release is completed. Furthermore, by reaching the window of the fenestrated stent graft, it can be verified if the openings of the brachiocephalic and the left subclavian arteries were correctly aligned against this window. In short, in this study, this "++" marked guidewire and the guidewire of the femoral artery formed a simple positioning system that was obviously beneficial to the release, positioning and verification of the fenestrated stent graft.

This study had several limitations but also improved several methods. Firstly, due to insufficient initial experimental time, limitations in supplies, and the special requirements of the animals required in this experiment, its sample size was small and seemed inadequately convincing. However, Experimental animals and stents are more expensive. More samples may be added appropriately to expand the sample size, depending on the conditions in the latter part of the experiment, which would increase the study's confidence and would validate the feasibility of applying EVAR treatment with fenestrated stent grafts for canine aortic arch trauma. However, according to Saari and others, this approach would not reduce confidence in the application of fenestrated stent grafts in the canine aortic arch. Secondly, the fenestrated stent grafts used in this experiment also have some limitations. They may be better indicated for breaches located on the small cursive side of the aortic arch and the anterior-posterior walls. Fenestrated stent grafts cannot be applied to arterial ruptures inside the "window" (e.g., in the branch vessels of the aortic arch). Thirdly, the methods chosen in this experiment would be increased the incidence of endoleak complications.

In summary, an ordinary straight-coated vascular stent that can be returned to the catheter and delivery sheath after fenestration in vitro and then made into a fenestrated stent graft for EVAR treatment of canine aortic arch trauma is technically feasible. This approach provides new ideas and an experimental basis for the clinical treatment of thoracic aortic trauma.

Acknowledgements

This work was supported by grants from 2010 military clinical high-tech funded plan projects (No. 2010 gxjs036) and the Wuhan General Hospital of Guangzhou Command funded plan (No. YZ201401).

Disclosure of conflict of interest

None.

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