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Original Article

Establishment of a dog aortic dissection model and treatment by film-covered stent grafting

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Abstract: This study aimed to establish a dog aortic dissection (AD) model, and to investigate the outcome of treatment using arterial film-covered stent grafting. The dog AD model was established using a traumatic method. Using an interventional method, film-covered stent grafting was performed to treat the AD lesion. The aorta and stents were removed 30 days later, and macroscopic examination and pathological and scanning electron microscopic (SEM) examination were conducted to observe the changes in the arterial intima and stents. The AD model was successfully established in 5 of 10 dogs, and was confirmed by computed tomography angiography (CTA). Among 5 successful AD models, 3 cases were implanted with the film-covered stent. The AD repair surgery was successful, and the animals recovered satisfactorily, with good survival conditions. CTA reexamination showed that the film-covered stent was fully released, tightly attaching to the aortic wall. The macroscopic, pathological, and SEM examinations all showed satisfactory treatment effect with film-covered stent grafting. Establishment of an AD model in the dog aorta is feasible, and the model is similar to the clinical lesion. Film-covered stent grafting has a satisfactory treatment effect for AD lesions.

Keywords: Aorta, dissection, stent, treatment

Introduction

In aortic dissection (AD), the aortic intimal wall ruptures due to a variety of reasons, and the blood flows into the mid-aortic wall. It is a disease with dangerous clinical manifestations and high mortality, and a challenge for clinical management [1]. In recent years, aortic endovascular repair has made breakthroughs in treating this disease [2], but there still are many problems to be considered [3-6], especially the changes in the arterial intima and stents [7-13]. Experimental studies on AD lesions and endovascular repair will help deepen understanding about the occurrence and development of this disease, thus improving clinical practice skills and endovascular repair results [14-17]. This experiment was conducted to establish an animal AD model, and film-covered stent grafting was then performed to treat the AD lesions. High-performance computed tomography (CT) and digital subtraction angiography (DSA) were used to examine the aortic intima and stents in AD, in order to study the changes related to aortic endovascular repair.

Methods

General information

Experimental animals: 10 hybrid dogs weighing 16-20 kg and without gender limitation were provided by the Experimental Animal Center of Chongqing Medical University, and fed by a designated caretaker according to the requirements for experimental animal feeding; the dogs were kept separate, at an ambient temperature of 18-25°C. The experimental site was the Chongqing Key Laboratory of Biomedical Engineering (State Key Laboratory). During the experiments, all animal procedures complied with ethical standards. This study was carried out in strict accordance with the recommendations in the Guide for the Care and Use of Laboratory Animals of the National Institutes of

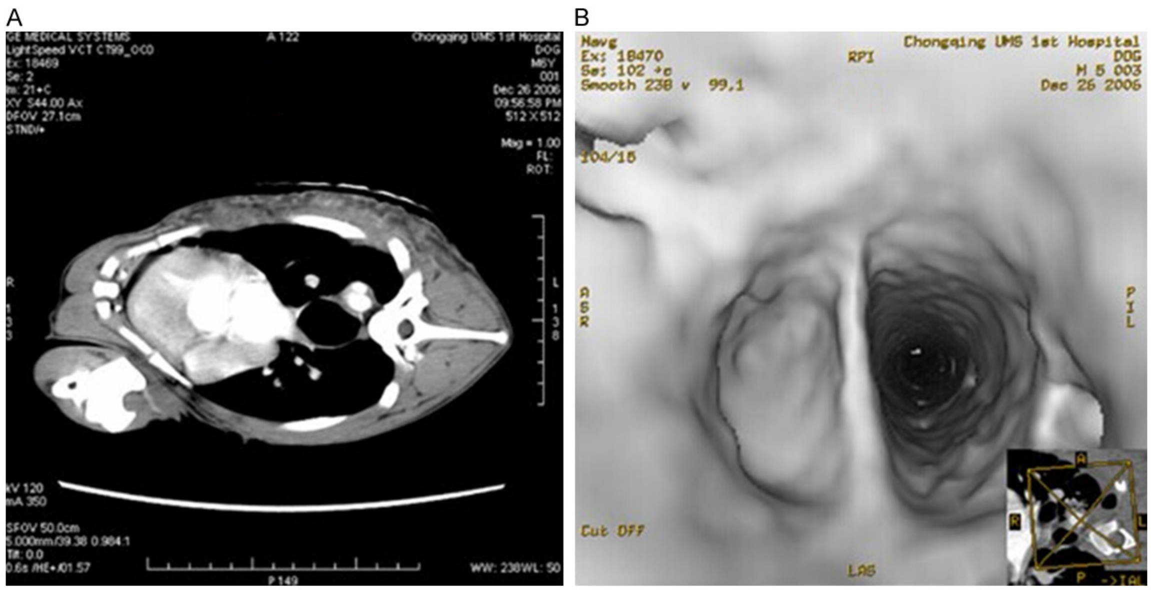

Figure 1. The pictures of dog aortic dissection (AD) in CT scan. A: CT image of AD; B: VE image of AD.

Health. The animal use protocol has been reviewed and approved by the Institutional Animal Care and Use Committee (IACUC) of Chongqing Medical University.

Method and model-preparing process

Anesthesia and thoracotomy: after an animal was anesthetized (2.5% sodium pentobarbital, 25 mg/kg), it was placed onto the operating table, intubated, and connected to an auxiliary breathing device (Dräger, Germany); routine surgical disinfection and towel paving were performed, followed by thoracotomy from the left 4-5 intercostal approach and thoracic cavity exposure layer by layer.

Modeling of AD lesion

After the descending aortic segment was exposed, a Satinsky vascular clamp was used to block about 1/2 of the descending aorta; the arterial adventitia was then carefully cut longitudinally for about 1 cm, and a stripping instrument (turbinate peeler) was inserted into the arterial intimal-external wall for membrane separation; a balloon (8 mm × 20 mm) was then inserted into the gap, and water-filled to widen it, so that the gap between the arterial walls was expanded; after insertion to about 10 cm, 2 ml elastase (500 U/L Shanghai Linzyme Biosciences Ltd., China) was injected into the balloon catheter and maintained for 30 min, until the balloon was withdrawn. After the artery was again blocked, the arterial intima in the surgical area was cut away (with an intimal flap measuring about 0.2 × 0.5 cm), and sutured with 6-0 propylene suture (Johnson & Johnson) to coincide with the outer membrane; minor bleeding at the anastomotic site was stopped with pressure or additional suturing.

Closure of thoracic cavity

After intrathoracic gas was removed, the chest was closed and the skin incisions were sutured; after surgery, the animals were fed in the animal center, and postoperative management was reinforced. CT angiography (CTA) (light speed VCT; GE Inc., USA) was performed 5-10 days after surgery to confirm the AD.

Grafting of film-covered stent

After the AD model had formed for 7-10 days, a film-covered stent (Vascore Medical Instrument Co., Ltd., China) was implanted. The experimental animal was anesthetized and fixed onto the operating table; after abdominal skin preparation, disinfection, and towel paving, an incision was performed approximately 15 cm below the midline of the inferior abdomen; the peritoneum was opened to expose the lower segment of the abdominal aorta, the inferior mesenteric artery was ligated, and the last segment of the abdominal aorta was selected to insert the

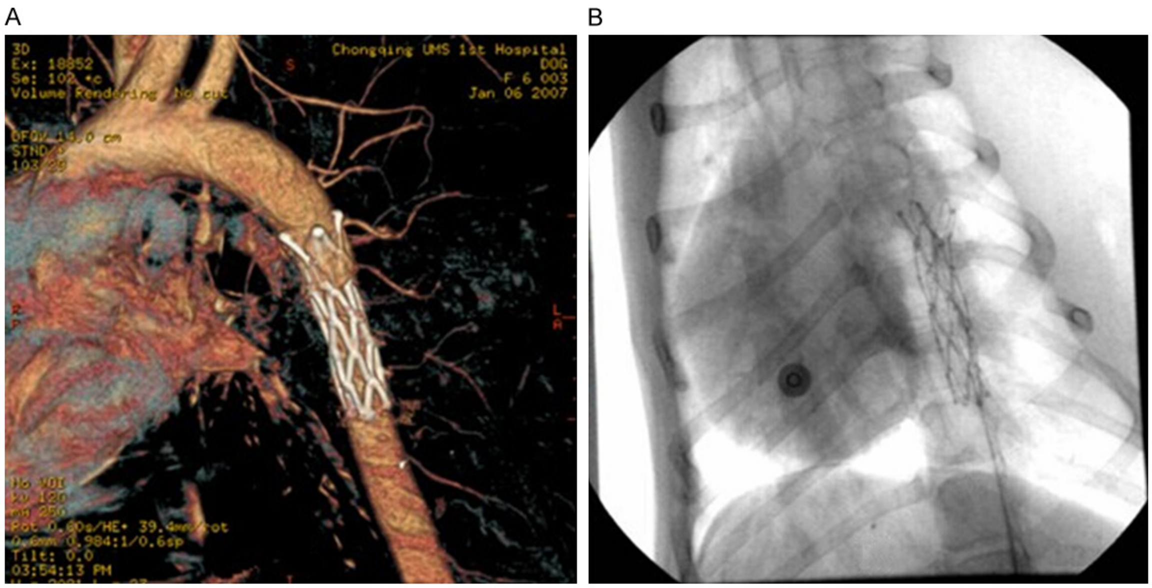

Figure 2. The pictures of the AD model after stent graft. A: CT (3DR) image of AD after the treatment; B: DSA image of AD (after the endovascular repair).

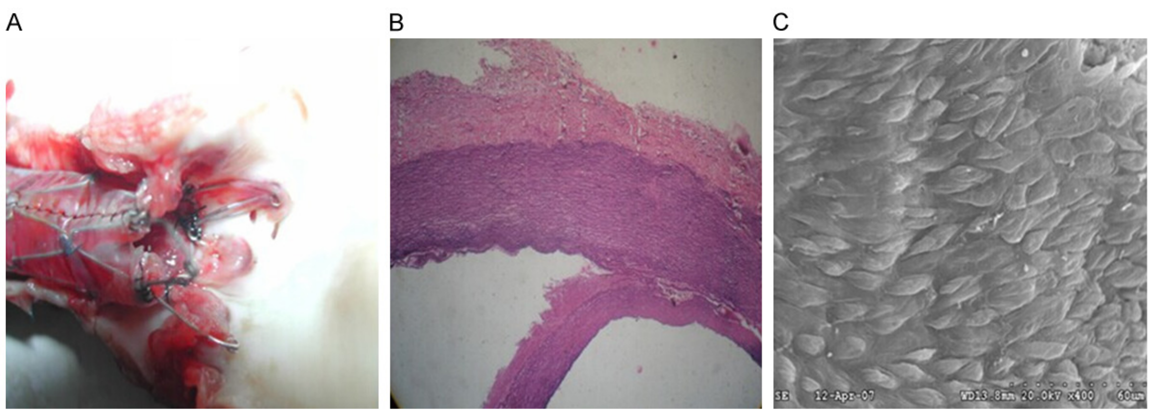

Figure 3. The pictures of gross specimen, pathological image and diseased intima in the AD model after stent graft. A: AD lesion and stent (gross specimen); B: Pathological image of AD (EF × 100); C: Diseased intima of AD (SEM × 400).

angiographic guidewire and catheter (DSA, Siemens Co); when angiography revealed the target lesion, a 15-F delivery system was used to import the stent, which was released and completely covered the AD crevasse after the target lesion was locked. A 6-0 propylene suture was then used on the arterial incision, followed by closure of the inferior peritoneum and abdomen. After surgery, the animals were fed in the animal experimental center. CTA was performed to review the AD lesions and repair effects. The animals were sacrificed 30 days later by anesthetic injection. The AD model specimens including the aorta and implanted arterial stent were removed; gross examination was performed, as well as pathological examination of the arterial intima with elastic fiber staining and scanning electron microscopy (SEM).

Results

Establishment of AD model

Among the 10 dogs in this experiment, the AD model was successfully established in 5, and was confirmed by CTA (**Figure 1A**, **1B**). The reasons for failure of AD model establishment were as follows: 1 death caused by lung injury during thoracotomy; 3 deaths from intraoperative hemorrhage during postoperative recovery; and 1 unexplained death after angiography.

Outcome of film-covered stent implantation

Among the 5 successful AD models, 3 were implanted with the film-covered stent. The AD repair surgery was successful, and the animals recovered satisfactorily, with good survival conditions. CTA reexamination showed that the film-covered stent was fully released, tightly attaching to the aortic wall. The dissection crevasse was closed completely, without leakage. The lumen was patent, showing no distortion or overlapping (**Figure 2A**, **2B**).

Results of macroscopic, pathological, and SEM examination

Macroscopic examination was performed on the aorta and stents. The stents were tightly attached to the arterial intima, and were difficult to separate (**Figure 3A**). Elastic fiber staining revealed an obvious and stable AD lesion in the arterial intima. SEM examination showed that the cord-like and regularly arranged arterial intimal endothelial cells extended along the vascular long axis, with a smooth surface, but no attachment. The nuclei swelled, without mural thrombi. The cellular gaps were uniformly small (**Figure 3B**, **3C**).

Discussion

The circulatory system of the dog is very similar to that of humans, and exhibited obvious advantages when used to produce the AD model [14-17]; it was also suitable for experiments on endovascular repair. This experiment mainly used a traumatic method to produce the lesions; when blood entered the dissection, the AD model obtained was stable, exhibiting characteristics similar to actual clinical changes. Based on this AD model, endovascular repair was performed, and could provide an experimental reference for clinical examination and treatment. It could also be used to observe changes in the arterial intima, as well as the performance and stability of arterial stents [18-20].

Film-covered stents used for clinical endovascular repair are mostly delivered and released through a femoral artery approach. The present experiment confirmed that the canine femoral artery (with a diameter mostly about 3 mm) could not be selected for a delivery approach under current equipment conditions. Therefore, this experiment used an abdominal aortic approach, which proved to be feasible. The experiment also highlighted requirements for the delivery system, such as further miniaturization; this could reduce the diameter of the system by reducing stent volume, so that the femoral or iliac artery would not be exposed clinically, thus achieving minimal invasion and leading to future improvements with this technique [21].

For AD detection and follow-up examination, CT provided strong technical support; details of changes in the arterial intima and stents were seen, showing the capabilities of current advanced detection equipment [22].

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Disclosure of conflict of interest

None.

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