Ann Thorac Cardiovasc Surg 2013; 19: 131–135

Online August 20, 2012
doi: 10.5761/atcs.oa.12.01948

*Original Article*

# A Canine Model of Proximal Descending Thoracic Aortic Aneurysm Created with an Autologous Pericardial Patch

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**Objectives: To establish an animal model of proximal descending thoracic aortic aneurysm for the study of branched stent grafts.**

**Materials and Methods: Eleven mongrel dogs underwent the surgical procedure during which an autologous pericardial patch was sewn onto a longitudinal incision in the anterolateral wall of the thoracic aorta near the left subclavian artery to create an artificial thoracic aortic aneurysm.**

**Results: All eleven animals survived the surgical procedure. One animal died from rupture at the surgical site during the first week after surgery. The distance between the artificial aneurysm and the left subclavian artery was 8.29 ± 0.91 mm. The average diameter of the artificial aneurysms did not significantly change over the 4-month follow-up period.**

**Conclusion: A canine model for proximal descending thoracic aortic aneurysm can be achieved using a safe and convenient method. The model can be used in the study of new branched stent graft applied to the aortic arch.**

**Keywords:** canine, animal model, pericardium, thoracic aortic aneurysm

## Introduction

The incidence of thoracic aorta aneurysms appears to be increasing.[1,2] Currently, treatments for thoracic aortic aneurysm include open surgical repair, hybrid surgery, and endovascular repair. Compared with open surgical repair, endovascular repair has lower procedure-related mortality and morbidity,[3–8] and it may be an alternative approach to open surgical repair.[5] However, the property of stent graft should be improved to overcome the inadequate flexibility, and endoleak.[9] Additionally, when aneurysms involving the aortic arch or the proximal end of descending thoracic aorta, the supra-aortic vessels of aortic arch have remained a challenge for endovascular repair.[10] Potentially, branched stent grafts could be developed to address these challenges. However, currently there is no animal model for thoracic aortic aneurysm suitable for studying these branched stent grafts. In this article, we describe a canine model for proximal descending thoracic aortic aneurysm created by using an autologous pericardial patch over a longitudinal incision in the anterolateral wall of the thoracic aorta near the left subclavian artery.

## Material and Methods

This study was approved by the Animal Care and Use

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Received: February 27, 2012; Accepted: March 19, 2012
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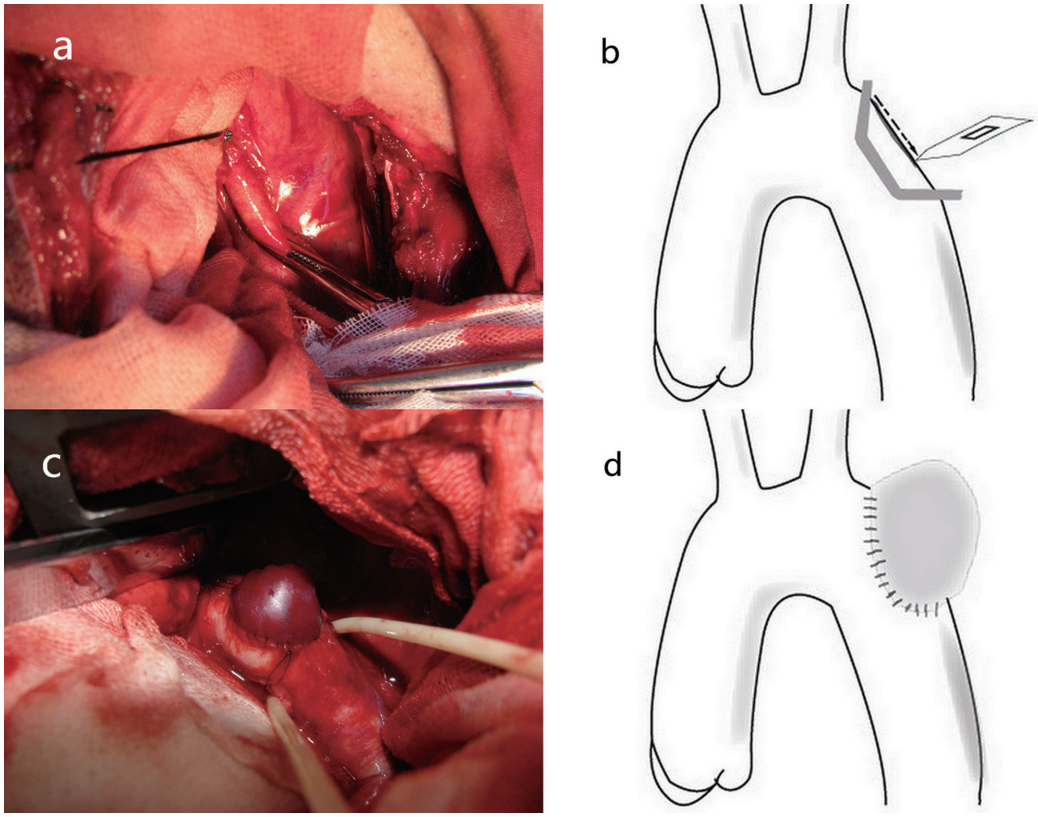


**Fig. 1** The surgical procedure for creating the aneurismal model. (**a, b**) The anterolateral wall of proximal descending thoracic aorta was clamped using an auricleclamp. A longitudinal incision was performed on the clamped thoracic aortic wall. (**c, d**) The pericardium patch was sewn onto the anterolateral side of the thoracic aorta.

Committee of China Medical University. Eleven adult mongrel dogs weighing 20.0–33.0 kg were provided by the Laboratory Animal Center of China Medical University.

After fasting for 12 h, the animals were anesthetized with intramuscular injection of Sumianxin at 0.1ml $kg^{-1}$ (Jilin Research and Development Center of Veterinary Drug, Jilin, China) and 3% pentobarbital sodium at 0.5ml $kg^{-1}$(Kefeng Chemical Reagent Co. LTD, Shanghai, China). Anesthesia was maintained with 0.5% halothane (Kefeng Chemical Reagent Co. LTD, Shanghai, China) under mechanical ventilation (AM100B; Yishiheng Co., Beijing, China). The dogs were fixed on the operating table in the right lateral position. The left chest was shaved. Venous access was established through the left hind leg.

Left thoracotomy was performed at the third-fourth intercostal space. A piece of pericardium was resected and was then fashioned into a 3- to 4-cm wide × 5- to 6-cm long oval patch. The proximal descending thoracic aorta was isolated. The anterolateral wall of the descending thoracic aorta was clamped using an auricleclamp without cessation of distal aortic flow. An approximately 3 cm incision was made in the clamped anterolateral wall of the descending thoracic aorta (**Fig.1a** and **1b**). The pericardial patches were oversized compared to the dimensions of the longitudinal aortotomy. This was purposely done to facilitate the formation of an aneurismal sac. The pericardial patch was sewn onto the longitudinal aortotomy using a continuous 5-0 polypropylene suture (**Fig. 1c** and **1d**) with the visceral surface of the patch on the aortic flow side. The auricleclamp was removed from the aorta. The distance between the artificial aneurysm and the left subclavian artery was measured with a vernier caliper. Finally, the thoracic cavity was closed. An enhanced computed tomography (CT) scan was performed (**Fig. 2**). The dogs were given penicillin sodium (1.6 million U per day by intramuscular injection) for 3 days following surgery.

Ten animals were followed for 4 months (one dog died from rupture at the surgical site during the first week after surgery). There were six time points of evaluation: the day before operation, the day of the operation, month

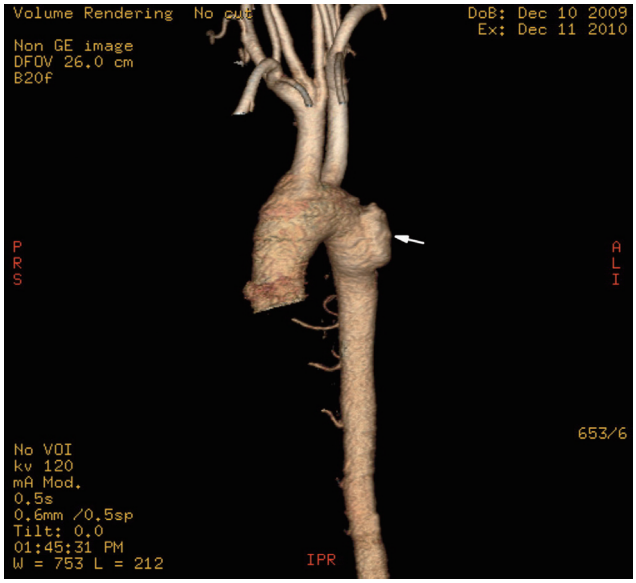


**Fig. 2** The volume rendering images of the aneurismal model (white arrow).

1, month 2, month 3, and month 4 after operation. Computed tomography angiography (CTA) examinations were performed on a 256-row CT scanner (Brilliance iCT, Philips, USA) in the craniocaudal direction to cover the entire body for each time point. Nonionic iodinated contrast agent (Optiray; Tyco Healthcare, Montreal, Quebec, Canada) was injected at a rate of 4ml/s by the use of a dual-syringe power injector (Ulrich Medizintechnik, Germany) for a total of 40–60 ml each time, and followed by 40 ml physiological saline at the same rate. The ascending aortic arch was set as the region of interest (ROI). The trigger threshold inside the ROI was set at 100 HU. The artificial aneurysms were visualized using volume rendering, and their maximal diameter was measured using commercial software (ADW 4.4; General Electric Company, USA).

At month 4, all the dogs were euthanized with 10% potassium chloride solution intravenously under general anesthesia. The segment of the thoracic aorta containing the artificial aneurysm was resected. The specimens were fixed in 10% formaldehyde solution and embedded in paraffin for histological examination using light microscopy after hematoxylin and eosin staining.

Statistical analysis was performed using SPSS 13.0 statistical software (SPSS, Inc., Chicago, IL). Numerical data are expressed as mean ± standard deviation. Changes in aneurysm diameter over time were analyzed using analysis of variance (ANOVA). $P < 0.05$ was considered statistically significant.

## Results

All 11 animals survived the surgical procedure, however, one animals died during the first week following the procedure. Autopsy revealed that the dog died from rupture at the suturing margin. There were no complications due to infarction of distal sites, paraplegia, or serious infection in the remaining animals during the follow-up period. The average operation time was 210 min (180–240 min). The average clamping time of the anterolateral wall was approximately 60 min (50–90 min). The average blood loss was 175 ml (150–250 ml) for each procedure.

The aneurysm created by the surgical procedure was saccular (**Fig. 2**). The distance between the aneurysm and the left subclavian artery was 8.29 ± 0.91 mm. On the day prior to the surgery, the mean maximal diameter of descending thoracic aorta at the planned surgical site was 15.75 ± 1.75 mm. Immediately following surgery, the mean, maximal diameter of the artificial aneurysm was 25.67 ± 2.43 mm. The diameter of this portion of the aorta was increased by 1.6 times on average by the procedure. The mean, maximal diameters at month 1, month 2, month 3, and month 4 were 26.43 ± 2.82 mm, 26.51 ± 2.81 mm, 26.41 ± 2.82 mm, and 26.34 ± 2.86 mm. There was no significant change in the maximal diameter of the postsurgical aorta from month 1 to 4 ($P > 0.05$).

On macroscopic examination, the pericardial patch was well incorporated into the aortic wall, and the suture line was well covered with the connective tissues at month 4 (**Fig. 3A**). The cavity of the artificial aneurysm was as smooth as the surrounding thoracic aortic wall. There were no thrombi observed in the cavity of the aneurysm (**Fig. 3B**). On microscopic examination, the pericardial patch was covered with mechanocyte and collagenous fiber. The inner surface of the aneurysm was covered with endotheliocyte (**Fig. 4**).

## Discussion

Various animal models of aortic aneurysm have been previously reported. The majority of these animal models are of aneurysms involving the abdominal aorta rather than the thoracic aorta.[11–13] Studies of creating animal models of thoracic aortic aneurysms were rare. Formichi et al. created animal models of thoracic aortic aneurysms in mongrel dogs using polyester patches.[14] Ikonomidis et al. used calcium chloride to create thoracic aortic aneurysms in mice.[15] Kajimoto et al. used jugular vein patches to create thoracic aortic aneurysms in beagles.[16] For

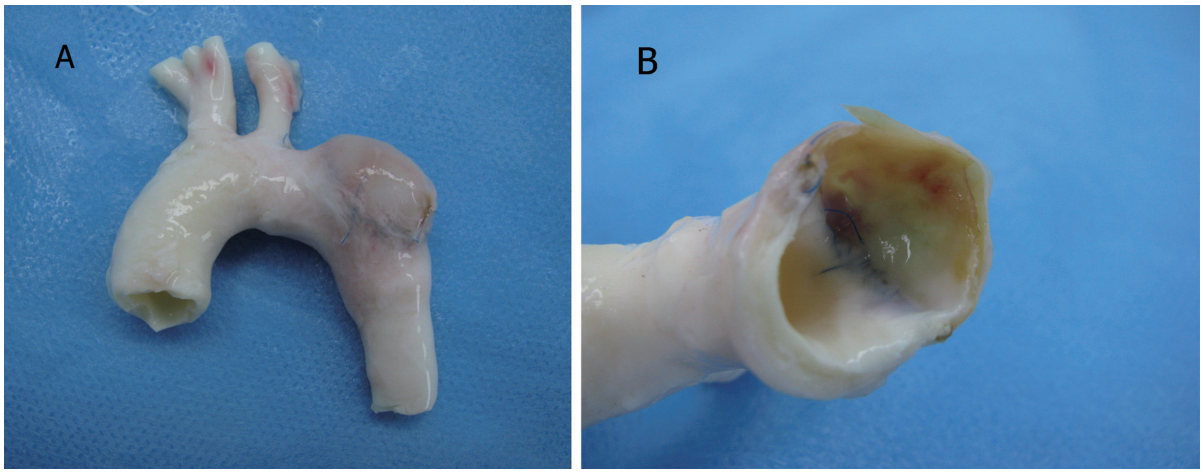


**Fig. 3** Specimens of the aneurismal model. (**A**) The pericardium patch was well incorporated with the aortic wall. The suture line was well covered with the proliferated tissue; (**B**) The aneurismal wall was as smooth as the thoracic aorta. There was no thrombus in the cavity of the aneurysm.

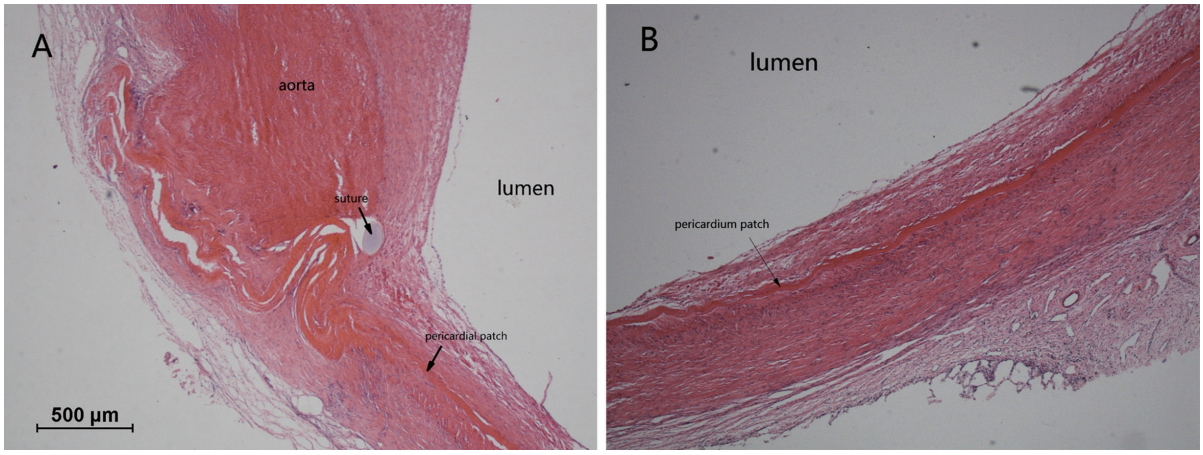


**Fig. 4** Light photomicrography of the aneurysm. (**A**) The inner and outer surface of the suturing margin was covered with mechanocyte and collagenous fiber. The suture was also visible (hematoxylin and eosin stain, × 40); (**B**) The inner and outer surface of the pericardium patch was covered with mechanocyte and collagenous fiber. The inner surface of the aneurismal was covered with endotheliocyte (hematoxylin and eosin stain, × 40).

successful stent graft placement, the proximal landing zone for the straight stent graft should be at least 20 mm in length.[17] If the distance between the aneurismal model and the left subclavian artery is less than 20 mm, the straight stent graft could not be used to treat the aneurysm, while the branched stent graft could overcome the challenge. Therefore, the aneurismal model suitable for the research of branched stent graft should be adjacent to or involve the left subclavian artery. Recently, all the animal models of thoracic aortic aneurysm were situated in the medial segment of the descending thoracic aorta,[14–16] while the average distance between our aneurismal model and the left subclavian artery was 8.29 ± 0.91 mm. Thus, the aneurismal model is suitable for the research of new branched stent grafts. Additionally, the prosthetic polyester patch used by Formichi et al could not imitate the structure of natural aortic aneurysm.[14] We created the aneurismal model by using autologous pericardium patch. Light photomicrography showed that the aneurismal wall was much thinner than the thoracic aorta; the pericardium patch was covered with mechanocyte and collagenous fiber; the inner surface of the aneurismal wall was covered with endotheliocyte. These characteristics are similar to the natural aneurysm. Mouse models of thoracic aortic aneurysm are too small for the research of endovascular technique.[15] While the canine model of

thoracic aortic aneurysm was ideal animal model for the research of endovascular technique for the suitable diameter of the artery, tolerance to surgical trauma. The acquirement of jugular vein patches by Kajimoto et al increased the extent of trauma and risk for infection.[16] In our surgical procedure, the left third-fourth intercostal thoracotomy could expose the proximal descending thoracic aorta and the pericardium sufficiently. Therefore, all the manipulation could be finished through the thoracotomy. Furthermore, the thoracic aorta was completely clamped in the surgical procedure of other aneurismal models.[14–16] That may increase the risk of distal infarction. We clamped the anterolateral wall of the thoracic aorta. The distal aortic flow of the thoracic aorta was not completely occluded. That could avoid the distal infarction.

In addition, during the follow-up period, there were no significant changes in the maximal diameter of the artificial aneurysms. Thus, the animal model of descending thoracic aortic aneurysm was stable for the extended study.

## Conclusion

We created a convenient, safe, and efficient method for creating animal models of proximal descending thoracic aortic aneurysm. Furthermore, this animal model imitates the characteristics and structure of natural aneurysms well and is suitable for studying new branched stent grafts applied to the aortic arch.

## Acknowledgements

This work was supported by the State Science and Technology Support Program of China [No. 2007BAI05B04] and the European Commission project Asia-Link CfP 2006-EuropeAid/123738/C/ACT/ Multi-Proposal [No. 128-498/111].

## Disclosure Statement

None.

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