Kaohsiung Journal of Medical Sciences (2013) 29, 194—199

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ORIGINAL ARTICLE

An experimental model of Stanford type B aortic dissection with intravenous epinephrine injection

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Received 5 September 2011; accepted 4 November 2011
Available online 11 January 2013

KEYWORDS
Aortic dissection;
Canine model;
Epinephrine;
Stanford type B

Abstract The aim of this study was to create an experimental model of aortic dissection (AD) with a long-term patent false lumen to develop new treatments for Stanford type B aortic dissection. Sixteen adult beagle dogs (weight 14—18 kg) were used. After exposure and partially clamping, the descending aorta was cut through the adventitia to one-third of the depth of the tunica media. The aortic wall was divided into two layers by raspatory. Then half the circumference of the inner layer was cut transversely. All of the proximal layers and the distal outer layers were anastomosed together. Epinephrine was immediately used to expand the false lumen, and the effect was terminated using nitroglycerin when necessary. All dogs underwent both digital subtraction angiography (DSA) and computed tomography angiography (CTA) immediately after and 1 week and 1 month after surgery. The dogs were followed up at 1 day, 3 months, 1 year, and 2 years. The surgery was successful in 12 dogs. Dissection formation was observed immediately after epinephrine administration and confirmed by DSA and CTA. Our results showed typical characteristics of AD, such as a tear, septum, and true and false lumens. This is an easy and feasible way of developing a Stanford type B AD model by intravenous injection of epinephrine. In this canine model of AD, the false lumen has excellent long-term patency and the dissection plane is histologically similar to that in human AD. This model may contribute to the development of new treatments for Stanford type B AD.

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http://dx.doi.org/10.1016/j.kjms.2012.08.033

Introduction

Aortic dissection (AD) is a potentially life-threatening condition in which there is bleeding into and along the wall of the aorta, the major artery carrying blood out of the heart; the survival rate of affected patients is low, irrespective of surgical or medical treatment [1—3]. AD is a frequently occurring pathology with a natural history, including a significant number of severe complications, including stroke, aortic valve insufficiency, cardiac tamponade, and aortic rupture.

AD is classified as type A or B. Type B AD initiates from the descending part of the aorta. Successful treatment of Stanford type B AD by intravascular stent grafts was first reported by Dake et al. in 1998 [4]. This endovascular technique is a mini-invasive, rapid, and effective treatment for AD. At present, it is the first treatment option for complicated type B AD and is used by vascular surgeons worldwide [5—7]. Various novel apparatuses for endovascular therapy have been developed and introduced [8—10]. Therefore, an ideal animal model for type B AD is required to investigate the effects of experimental treatments and pathological changes in this condition over time.

Current methods for development of an AD animal model are complex, time-consuming, and difficult to follow, or are not similar to the characteristics of typical human AD [11—16]. In this paper, we describe an easy method of developing a canine Stanford type B AD model by intravenous injection of epinephrine.

Materials and methods

Animals

Sixteen beagle dogs (weight 14.0—18.0 kg) provided by the Laboratory Animal Center of Zhongshan Hospital were used. The study was approved by the Institutional Animal Care and Use Committee.

Surgical methods

Each dog was fixed in the right lateral position on an operating table. The skin of the left chest and thigh was shaved, and antibiotics were administered through an intravenous access point that was established through the tongue. The right femoral artery was intubated for direct blood pressure monitoring. General anesthesia was administered using intravenous 2.5% sodium pentothal (1 mg/kg); mechanical ventilation was then applied via tracheal intubation. During surgery, anesthesia was maintained with 1 ± 1.5% isoflurane under mechanical ventilation.

An incision was made at the third and fourth intercostal space to access the thoracic cavity. Then the descending thoracic aorta and the left innominate artery (LIA) were carefully exposed by severing the surrounding soft tissues. Two or three pairs of intercostal arteries were ligated to prevent bleeding during anastomosis. To facilitate aortic suspension and prevent possible excessive intraoperative hemorrhaging, two plastic blocking bands were placed, one around the portion of the descending aorta immediately distal to the LIA origin and the other ~4 cm distal to the first one. After systemic heparin infusion (100 IU/kg), the descending aorta was partially clamped using the blocking bands and the proximal part of the aorta was suspended to facilitate surgery. The portion of the descending aorta immediately distal to the LIA origin was carefully cut transversely through the adventitia up to approximately one-third of the depth of the tunica media, along one-third of the aortic circumference. Subsequently, a raspatory was used to divide the aortic wall into an inner and an outer layer and thus formed a small dissection. The outer layer consisted of the adventitia and the tunica media up to approximately one-third of its original width. The descending aorta was secured completely using two clamps, one placed proximal and the other distal to the incision. Then the inner layer was cut open transversely along half of its circumference, and part of the distal inner layer was trimmed off. All layers proximal to the incision and the outer layer distal were anastomosed together using a 6/0 prolene suture to ensure that blood flowed into the false lumen.

Subsequently, 0.05 mg/kg epinephrine was injected via the peripheral vein to increase the blood pressure and pressure gradient. As the blood pressure increased, the dissection immediately enlarged and propagated distally. To avoid vascular rupture, this expansive effect was eliminated by administrating nitroglycerin when the dissection extended beyond the level of the diaphragm. The blood pressure was monitored by electrocardiography before and after epinephrine and after nitroglycerin injection. The thoracic wall was closed and the dissection formation was completed (Fig. 1). Each experimental animal underwent digital subtraction angiography (DSA) immediately after the operation. All surviving animals underwent magnetic resonance angiography (MRA) or computed tomography angiography (CTA) 1 week or 1 month later. Blood vessels were stained with hematoxylin and eosin, elastica van Gieson, and azan stain.

Results

Sixteen dogs underwent surgery. Of these, four died during the operation due to aortic rupture ($n = 2$), sudden unexplained cardiac arrest ($n = 1$), or anesthetic drug overdose ($n = 1$). Mean blood pressure before and after epinephrine injection and after nitroglycerin injection were 149.5 ± 7.3/86.7 ± 9.1 mmHg, 189.3 ± 22.5/124.5 ± 19.5 mmHg, and 123.1 ± 11.7/84.5 ± 8.9 mmHg, respectively. Among the 12 dogs that survived, one developed paraplegia on the second postoperative day, one had ischemia of the hind limbs and died of ulceration and infection 2 weeks later, and one had bowel ischemia and died 1 week later.

The other nine dogs were reared for a certain period. DSA (Fig. 2), performed immediately after the procedure, and CTA (Fig. 3), performed 1 week or 1 month later, showed that the false lumen was patent. The morphology of the dissection was typical. After euthanasia, the true and false lumens of the aorta were clearly observed (Fig. 4). Microscopic examination showed that the dissection created during surgery was located in the medial layer of the aorta. It was similar to the AD that usually occurs in